

“Pharmacy on Demand” To Revolutionize Drug Manufacturing and Care Delivery

A device, titled a “*pharmacy on demand*,” is capable of producing 1,000 distinct pharmaceutical drugs, with the device being tested on generic drugs to start, in a 24-hour period.¹ The *Massachusetts Institute of Technology* (MIT), in conjunction with the *Defense Advanced Research Projects Agency* (DARPA),² recently developed a device with the potential to revolutionize the pharmaceutical industry by condensing the time and steps required to manufacture drugs. The current prototype consists of reconfigurable components, e.g., reactors, precipitation tanks, and filtration and crystallization units, that are added or removed depending on the drug being created.³ The current iteration of the device, which is the size of a standard kitchen refrigerator, utilizes *continuous manufacturing techniques*, which eliminates many of the steps required to create pharmaceuticals under traditional *batch processing methods*.⁴ Recent developments suggest that this device may eventually be located in military battlefield hospitals, hard to reach areas, traditional hospitals, and pharmacies,⁵ as researchers have demonstrated the device’s current capabilities to produce pharmaceuticals commonly utilized in an inpatient setting, including Benadryl, Valium, Prozac, and a local anesthetic.⁶ This *Health Capital Topics* article will discuss the advent of this new technology, and briefly detail recent initiatives by private and public entities for expanding the use of continuous manufacturing techniques, such as the “*pharmacy on demand*,” as well as, the differences between *continuous* and *batch* manufacturing.

Until the introduction of *continuous manufacturing*, the only viable option for most pharmaceutical drug manufacturers was using the *batch processing method*,⁷ the production of pharmaceuticals in which “...*batches of chemicals are synthesized, then... cool[ed] down, then are synthesized again to create new compounds*.”⁸ Subsequently, the compounds created under batch processing must crystallize, filter, and dry, and then powder is added to create a tablet or capsule.⁹ Generally, the synthesis of chemicals and the subsequent creation into a tablet or capsule occur in separate facilities, and the entire process can take months to complete.¹⁰ In contrast, the *continuous manufacturing method* integrates the steps under batch manufacturing, and the processes “...*allow for raw materials to be input[ed] into the system and the finished product to be discharged from the system in a*

continuous fashion.”¹¹ In this type of pharmaceutical manufacturing process:

“...[A] *continuous-flow process enables integration of reaction, crystallization, purification, and formulation with advanced control and realtime monitoring capabilities, thus enabling the application of quality-by-design principles and miniaturization of the entire end-to-end manufacturing platform*.”¹²

The *Department of Defense* (DOD) has sought to advance continuous manufacturing in medicine in order to improve military access to pharmaceuticals commonly utilized in battlefield medicine. DARPA, in collaboration with MIT, assists in developing continuous manufacturing techniques with the goal of utilizing this technology in:

- (1) Field hospitals for military service personnel;
- (2) Remote areas during disease outbreaks; and,
- (3) Other strategic locations in the U.S.,¹³ which may include:
 - (a) Minimizing effects of drug shortages;
 - (b) Filling gaps in the orphan drug market;
 - (c) Assisting in the advancement of precision medicine by creating drugs tailored to specific biomarkers related to disease; and,
 - (d) Enhancing medication access to underserved areas, both nationally and internationally.¹⁴

To achieve these goals, DARPA’s continuous manufacturing programs, *Pharmacy on Demand* (PoD) and *Biologically-derived Medicines on Demand* (Bio-MOD), aim to create portable devices capable of producing multiple *U.S. Food and Drug Administration* (FDA)-approved drugs within a 24-hour timeframe.¹⁵ Current production rates of the PoD, within a 24 hour timeframe, are: 21,900 doses of Diphenhydramine; 2,596 doses of Lidocaine; 19,500 doses of Diazepam; 5,000 doses of Fluoxetine; 1,547 doses of Ibuprofen; 1,000,000 doses of Atropine; and, 1,200 doses of Doxycycline.¹⁶

During a recent St. Louis conference sponsored by the St. Louis Chapter of the American Society of Appraisers, Geoff Ling, M.D., Ph.D., FANA, FAAN (U.S. Army Col., Ret.), former director of the Biological

Technologies Office of DARPA, co-presented with HCC CEO Robert James Cimasi, MHA, ASA, FRICS, MCBA, CVA, CM&AA, on current and future technological developments in the healthcare industry, and discussed the benefits of this evolving technology in both military and civilian applications. Dr. Ling noted that PoDs may reduce the potential for “*drug shortages*” and “*orphan drugs*,” while also “*enhanc[ing] disaster responsiveness*” and providing “*cost and storage space savings*.”¹⁷

In addition to public sector investment in continuous manufacturing techniques for pharmaceuticals, many private sector companies in the pharmaceutical industry have begun to utilize this technique to produce their products. The effort to implement continuous manufacturing in the pharmaceutical industry began in 2007, when Novartis partnered with MIT for assistance in the company’s transition away from traditional batch processes.¹⁸ This effort has since expanded, with other companies contributing to the initiative of implementing continuous manufacturing techniques into company practice. On April 8, 2016, *Johnson & Johnson* (J&J) received approval from the FDA to switch their manufacturing process from *batch* to *continuous* in creating Prezista, a drug it produces for HIV-1 treatment.¹⁹ Within eight years, J&J hopes to manufacture 70% of its highest-volume products through a continuous manufacturing process.²⁰ Vertex shifted to continuous manufacturing in July 2015 for Orkambi, a drug it produces for cystic fibrosis.²¹ *GlaxoSmithKline* (GSK) invested over \$50 million in continuous manufacturing to manufacture amoxicillin for Augmentin, finding that the new technique “*...allows medicine to be made cheaper, faster, and with a smaller impact on the environment*.”²² Additionally, Pfizer entered into a collaborative arrangement with GSK in October 2015 to upgrade Pfizer’s previously-constructed continuous manufacturing system.²³

In April 2016, the FDA endorsed utilizing this new manufacturing process, finding that “*...by eliminating breaks between steps and reducing opportunities for human errors during the stops and starts in the batch process, continuous manufacturing is more reliable — and safer*” than traditional batch processing methods.²⁴ The FDA has cited certain advantages in continuous manufacturing that may lead to reduced healthcare costs, including: (1) shorter processing times by eliminating time-consuming steps in the manufacturing process; (2) smaller equipment and facilities to produce pharmaceuticals; and, (3) on-line monitoring for quality control.²⁵ In general, “[*the*] FDA will continue [*its*] efforts to encourage the advancement of continuous manufacturing as one of a variety of ways to enhance the quality of the medications used by the American public.”²⁶

However, implementing continuous manufacturing in the pharmaceutical industry may have certain drawbacks. Specifically, pharmaceutical companies have cited potential issues regarding intellectual

property rights and patient safety stemming from the utilization of portable pharmacies.²⁷ Drug manufacturers typically enjoy exclusive production rights to drugs they created for three to five years following development,²⁸ and portable pharmacies have the potential to intrude on those intellectual property rights by allowing the production of drugs outside of this exclusive right.²⁹ On the issue of patient safety, the FDA noted various concerns regarding the guarantee of patient safety with drugs produced from portable pharmacies, including: (1) the need to integrate analytical tools that implement feedback mechanisms based on data gathered by the device; (2) the defining of representative sampling to ensure drug quality over time; and, (3) an incomplete understanding of the continuous manufacturing process.³⁰ Since noting its concerns, the FDA has supported implementing continuous manufacturing by utilizing a science and risk-based approach,³¹ as well as establishing the *Emerging Technology Team* (ETT) to “*...work[] directly with [the pharmaceutical] industry to help identify and resolve scientific issues for new technologies*.”³²

While public sector agencies and private pharmaceutical companies have been at the forefront of developing and implementing continuous manufacturing, hospitals and pharmacies may also be significantly impacted by this new technology. For example, hospitals and pharmacies may implement portable pharmacies for emergency purposes;³³ just as emergency electrical generators alleviate issues caused by power outages, pharmacies or hospitals may use portable pharmacies to help alleviate drug shortages during disease outbreaks and high trauma volume.³⁴ Other potential benefits, such as avoiding the need for refrigeration, as well as avoiding dependency on single source manufacturers,³⁵ may help steer such organizations toward implementing this new technology.

Additionally, portable pharmacies may also impact the acceleration of the shift toward personalized medicine. The FDA noted, “[*w*]e are entering an era of precision medicine, when drugs must be made with unique features and provided more quickly to patients in need.”³⁶ Notable researchers believe that these objectives may be furthered by portable pharmacies.³⁷ Healthcare industry stakeholders may choose to follow the advancements of this evolving portable pharmacy technology, as it has the potential to create a disruption in the pharmaceutical industry, while also providing pharmacies and hospitals with additional avenues in implementing drug processing.

-
- 1 “Inventing a Machine That Spits Out Drugs in a Whole New Way” By Martha Bebinger, HealthLeaders Media, May 26, 2016, <http://www.healthleadersmedia.com/technology/inventing-machine-spits-out-drugs-whole-new-way> (Accessed 6/1/16).
 - 2 MIT is a research university, and had a fiscal year 2015 budget for research of \$2.2 billion; DARPA develops emerging technologies for the military, and had a fiscal year 2015 budget for research, development, testing, and evaluation of \$2.91 billion.

- 3 "On-demand continuous-flow production of pharmaceuticals in a compact, reconfigurable system" By Andrea Adamo, et al., American Association for the Advancement of Science, April 1, 2016, Vol. 352, No. 1681, p. 62.
- 4 Bebinger, May 26, 2016.
- 5 "Inventing a Machine That Spits Out Drugs in a Whole New Way" By Martha Bebinger, HealthLeaders Media, May 26, 2016, <http://www.healthleadersmedia.com/technology/inventing-machine-spits-out-drugs-whole-new-way> (Accessed 6/1/16).
- 6 "Compact drug synthesizer could revolutionize drug delivery" American Association for the Advancement of Science, March 31, 2016, http://www.eurekalert.org/pub_releases/2016-03/aaf-cds032816.php (Accessed 6/7/17).
- 7 Bebinger, May 26, 2016.
- 8 *Ibid.*
- 9 *Ibid.*
- 10 "Pharmacy on demand: New technologies to enable miniaturized and mobile drug manufacturing" By John Lewin, Eugene Choi, and Geoffrey Ling, American Journal of Health-System Pharmacy, Vol. 73, No. 2 (January 15, 2016), p. 48.
- 11 "Promoting Continuous Manufacturing in the Pharmaceutical Sector" Brookings, October 19, 2015, <http://www.brookings.edu/~media/events/2015/10/19-continuous-manufacturing-pharmaceutical-sector/continuous-manufacturing-discussion-guide.pdf> (Accessed 6/1/16), p. 1.
- 12 Lewin, Choi, and Ling, January 15, 2016, p. 48-9.
- 13 Bebinger, May 26, 2016; "Battlefield Medicine" By Dr. Tyler McQuade, Defense Advanced Research Projects Agency, <http://www.darpa.mil/program/battlefield-medicine> (Accessed 6/1/16).
- 14 Lewin, Choi, and Ling, January 15, 2016, p. 45.
- 15 *Ibid.*, p. 46.
- 16 "Health Care's New Horizon" Geoffrey Ling, M.D., Ph.D., FANA, FAAN, American Society of Appraisers Healthcare Special Interest Group's Multidisciplinary Advanced Education in Healthcare Valuation Program: St. Louis, MO, May 7, 2016, slide 37.
- 17 Ling, May 7, 2016, slide 36.
- 18 "Continuous drug manufacturing offers speed, lower costs" By Anne Trafton, Massachusetts Institute of Technology News, March 12, 2012, <http://news.mit.edu/2012/manufacturing-pharmaceuticals-0312> (Accessed 6/1/16).
- 19 "Continuous Manufacturing Has a Strong Impact on Drug Quality" By Lawrence Yu, Food and Drug Administration, April 12, 2016, <http://blogs.fda.gov/fdavoices/index.php/2016/04/continuous-manufacturing-has-a-strong-impact-on-drug-quality/> (Accessed 6/1/16).
- 20 "FDA Approves Tablet Production on Continuous Manufacturing Line" Engineering Research Centers, <http://erc-assoc.org/content/fda-approves-tablet-production-continuous-manufacturing-line-0> (Accessed 6/1/16).
- 21 Yu, April 12, 2016.
- 22 "Less is more with advanced technologies in manufacturing" GlaxoSmithKline, October 7, 2015, <http://www.gsk.com/en-gb/behind-the-science/how-we-do-business/less-is-more-with-advanced-technologies-in-manufacturing/> (Accessed 6/1/16); "GSK investing \$60m in greener manufacturing at Singapore amoxicillin plant" By Dan Stanton, In-PharmaTechnologist, July 1, 2015, <http://www.in-pharmatechnologist.com/Processing/GSK-investing-60m-in-greener-manufacturing-at-Singapore-plant> (Accessed 6/8/16).
- 23 "Pfizer Announces Collaboration With GSK On Next-Generation Design Of Portable, Continuous, Miniature And Modular (PCMM) Oral Solid Dose Development And Manufacturing Units" Pfizer, October 29, 2015, <http://www.pfizer.com/news/press-release/press-release-detail/pfizer-announces-collaboration-with-gsk-on-next-generation-design-of-portable-continuous-miniature-and-modular-pcmm-oral-solid-dose-development-and-manufacturing-units> (Accessed 6/1/16).
- 24 Yu, April 12, 2016.
- 25 "FDA Perspective on Continuous Manufacturing" By Sharmista Chatterjee, Food and Drug Administration, January 2012, <http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM341197.pdf> (Accessed 6/1/16), p. 8.
- 26 *Ibid.*
- 27 Bebinger, May 26, 2016.
- 28 "New drug product exclusivity" 21 C.F.R. § 314.108(b) (1994).
- 29 *Ibid.*
- 30 Chatterjee, January 2012, p. 19.
- 31 *Ibid.*, p. 20.
- 32 "Modernizing Pharmaceutical Manufacturing to Improve Drug Quality: Ensuring a Safe and Adequate Supply of Drugs" By Michael Kopcha, Food and Drug Administration, February 1, 2016, <http://blogs.fda.gov/fdavoices/index.php/2016/02/modernizing-pharmaceutical-manufacturing-to-improve-drug-quality-ensuring-a-safe-and-adequate-supply-of-drugs/> (Accessed 6/8/16).
- 33 "Pharmacy on demand: New, portable system can be configured to produce different drugs" By Anne Trafton, Massachusetts Institute of Technology News, March 31, 2016, <http://news.mit.edu/2016/portable-pharmacy-on-demand-0331> (Accessed 6/2/16).
- 34 *Ibid.*
- 35 Ling, May 7, 2016, slide 36.
- 36 Yu, April 12, 2016.
- 37 "Going with the flow: A desktop machine allows on-demand medicine production" By Rainer Martin, American Association for the Advancement of Science, Vol. 352, No. 6281 (April 1, 2016), p. 1; "On-Demand Drug Production Is on the Horizon" By Bob Roehr, Scientific American, April 1, 2016, <http://www.scientificamerican.com/article/on-demand-drug-production-is-on-the-horizon/> (Accessed 6/1/16).

HEALTHCARE VALUATION
THE FINANCIAL APPRAISAL OF
ENTERPRISES, ASSETS, AND SERVICES
Robert James Cimasi, MHA, ASA, FRICS, MCBA, AVA, CM&AA – CEO, HEALTH CAPITAL CONSULTANTS
Foreword by Shannon P. Frail
“...the definitive treatise for the complexities of valuation in the healthcare industry.”
- Chris M. Mellen, President - Delphi Valuation Advisors, Inc.

The Adviser's Guide to Health Care
Robert James Cimasi, MHA, ASA, FRICS, MCBA, AVA, CM&AA – CEO, HEALTH CAPITAL CONSULTANTS
Todd A. Zigrang, MBA, MHA, FACHE, ASA – President, HEALTH CAPITAL CONSULTANTS
AICPA
Keep Up With the Changes in Health Care Services and Consulting Practices
Includes Foreword by Leading National Health Care Attorney
David W. Graiser, Esq., Partner - Jones Day
TWO-VOLUME SET
• Consulting Services
• An Era of Reform - The Four Pillars
To purchase, visit AICPAStore.com/AGHC

ACOs: Balancing Quality and Costs in Healthcare
Robert James Cimasi, MHA, ASA, FRICS, MCBA, AVA, CM&AA – CEO, HEALTH CAPITAL CONSULTANTS
Foreword by Peter A. Pavarni, Esq. – Squire Sanders LLP
“A must read and resource for any healthcare industry executive”
—Roger W. Logan, MS, CPA/ABV, ASA, Senior Vice President of Phoenix Children's Hospital
Learn more at CRCPress.com



(800) FYI - VALU

*Providing Solutions
in the Era of
Healthcare Reform*

Founded in 1993, HCC is a nationally recognized healthcare economic financial consulting firm

- [HCC Home](#)
- [Firm Profile](#)
- [HCC Services](#)
- [HCC Experts](#)
- [Clients & Projects](#)
- [HCC News](#)
- [Upcoming Events](#)
- [Contact Us](#)
- [Email Us](#)

HEALTH CAPITAL

CONSULTANTS (HCC) is an established, nationally recognized healthcare financial and economic consulting firm headquartered in St. Louis, Missouri, with regional personnel nationwide. Founded in 1993, HCC has served clients in over 45 states, in providing services including: valuation in all healthcare sectors; financial analysis, including the development of forecasts, budgets and income distribution plans; healthcare provider related intermediary services, including integration, affiliation, acquisition and divestiture; Certificate of Need (CON) and regulatory consulting; litigation support and expert witness services; and, industry research services for healthcare providers and their advisors. HCC's accredited professionals are supported by an experienced research and library support staff to maintain a thorough and extensive knowledge of the healthcare reimbursement, regulatory, technological and competitive environment.



Robert James Cimasi, MHA, ASA, FRICS, MCBA, CVA, CM&AA, serves as Chief Executive Officer of **HEALTH CAPITAL CONSULTANTS (HCC)**, a nationally recognized healthcare financial and economic consulting firm headquartered in St. Louis, MO, serving clients in 49 states since 1993. Mr. Cimasi has over thirty years of experience in serving clients, with a professional focus on the financial and economic aspects of healthcare service sector entities including: valuation consulting and capital formation services; healthcare industry transactions including joint ventures, mergers, acquisitions, and divestitures; litigation support & expert testimony; and, certificate-of-need and other regulatory and policy planning consulting.

Mr. Cimasi holds a Master in Health Administration from the University of Maryland, as well as several professional designations: Accredited Senior Appraiser (ASA – American Society of Appraisers); Fellow Royal Institution of Chartered Surveyors (FRICS – Royal Institution of Chartered Surveyors); Master Certified Business Appraiser (MCBA – Institute of Business Appraisers); Accredited Valuation Analyst (AVA – National Association of Certified Valuators and Analysts); and, Certified Merger & Acquisition Advisor (CM&AA – Alliance of Merger & Acquisition Advisors). He has served as an expert witness on cases in numerous courts, and has provided testimony before federal and state legislative committees. He is a nationally known speaker on healthcare industry topics, and is the author of several books, the latest of which include: “*Adviser’s Guide to Healthcare – 2nd Edition*” [2015 – AICPA]; “*Healthcare Valuation: The Financial Appraisal of Enterprises, Assets, and Services*” [2014 – John Wiley & Sons]; “*Accountable Care Organizations: Value Metrics and Capital Formation*” [2013 - Taylor & Francis, a division of CRC Press]; and, “*The U.S. Healthcare Certificate of Need Sourcebook*” [2005 - Beard Books].

Mr. Cimasi is the author of numerous additional chapters in anthologies; books, and legal treatises; published articles in peer reviewed and industry trade journals; research papers and case studies; and, is often quoted by healthcare industry press. In 2006, Mr. Cimasi was honored with the prestigious “*Shannon Pratt Award in Business Valuation*” conferred by the Institute of Business Appraisers. Mr. Cimasi serves on the Editorial Board of the Business Appraisals Practice of the Institute of Business Appraisers, of which he is a member of the College of Fellows. In 2011, he was named a Fellow of the Royal Institution of Chartered Surveyors (RICS).



Todd A. Zigrang, MBA, MHA, ASA, FACHE, is the President of **HEALTH CAPITAL CONSULTANTS (HCC)**, where he focuses on the areas of valuation and financial analysis for hospitals, physician practices, and other healthcare enterprises. Mr. Zigrang has over 20 years of experience providing valuation, financial, transaction and strategic advisory services nationwide in over 1,000 transactions and joint ventures. Mr. Zigrang is also considered an expert in the field of healthcare compensation for physicians, executives and other professionals.

Mr. Zigrang is the co-author of the “*Adviser’s Guide to Healthcare – 2nd Edition*” [2015 – AICPA], numerous chapters in legal treatises and anthologies, and peer-reviewed and industry articles such as: *The Accountant’s Business Manual* (AICPA); *Valuing Professional Practices and Licenses* (Aspen Publishers); *Valuation Strategies; Business Appraisal Practice*; and, *NACVA QuickRead*. In addition to his contributions as an author, Mr. Zigrang has served as faculty before professional and trade associations such as the American Society of Appraisers (ASA); the National Association of Certified Valuators and Analysts (NACVA); Physician Hospitals of America (PHA); the Institute of Business Appraisers (IBA); the Healthcare Financial Management Association (HFMA); and, the CPA Leadership Institute.

Mr. Zigrang holds a Master of Science in Health Administration (MHA) and a Master of Business Administration (MBA) from the University of Missouri at Columbia. He is a Fellow of the American College of Healthcare Executives (FACHE) and holds the Accredited Senior Appraiser (ASA) designation from the American Society of Appraisers, where he has served as President of the St. Louis Chapter, and is current Chair of the ASA Healthcare Special Interest Group (HSIG).



John R. Chwarzinski, MSF, MAE, is Senior Vice President of **HEALTH CAPITAL CONSULTANTS (HCC)**. Mr. Chwarzinski’s areas of expertise include advanced statistical analysis, econometric modeling, as well as, economic and financial analysis. Mr. Chwarzinski is the co-author of peer-reviewed and industry articles published in *Business Valuation Review* and *NACVA QuickRead*, and he has spoken before the Virginia Medical Group Management Association (VMGMA) and the Midwest Accountable Care Organization Expo.

Mr. Chwarzinski holds a Master’s Degree in Economics from the University of Missouri – St. Louis, as well as, a Master’s Degree in Finance from the John M. Olin School of Business at Washington University in St. Louis. He is a member of the St. Louis Chapter of the American Society of Appraisers, as well as a candidate for the Accredited Senior Appraiser designation from the American Society of Appraisers.



Jessica L. Bailey-Wheaton, Esq., is Vice President and General Counsel of **HEALTH CAPITAL CONSULTANTS (HCC)**, where she conducts project management and consulting services related to the impact of both federal and state regulations on healthcare exempt organization transactions and provides research services necessary to support certified opinions of value related to the Fair Market Value and Commercial Reasonableness of transactions related to healthcare enterprises, assets, and services. Ms. Bailey is a member of the Missouri and Illinois Bars and holds a J.D., with a concentration in Health Law, from Saint Louis University School of Law, where she served as Fall Managing Editor for the *Journal of Health Law & Policy*.



Kenneth J. Farris, Esq., is a Research Associate at **HEALTH CAPITAL CONSULTANTS (HCC)**, where he provides research services necessary to support certified opinions of value related to the Fair Market Value and Commercial Reasonableness of transactions related to healthcare enterprises, assets, and services, and tracks impact of federal and state regulations on healthcare exempt organization transactions. Mr. Farris is a member of the Missouri Bar and holds a J.D. from Saint Louis University School of Law, where he served as the 2014-2015 Footnotes Managing Editor for the *Journal of Health Law & Policy*.