Exchange

CARLSON SCHOOL OF MANAGEMENT
UNIVERSITY OF MINNESOTA

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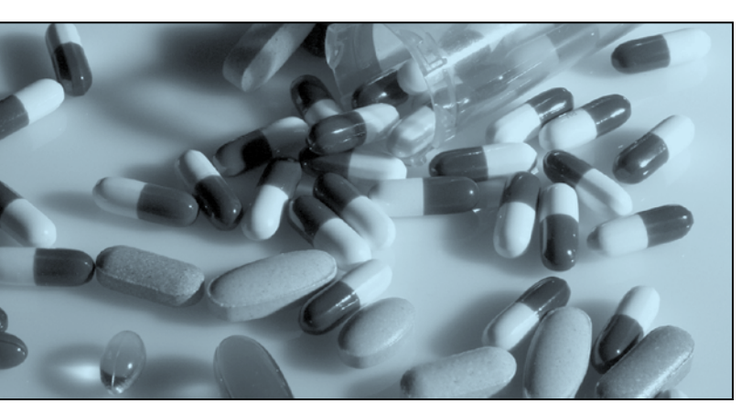
Better, But for How Long?

It all started with a Juran Quality Summit some nine years ago. Carlson School Associate Professor Enno Siemsen and his colleagues spotted one emergent issue: were quality capabilities sustainable?

Siemsen says that, at the same time, colleague John Gray, now at Ohio State University, gained access to a unique inspection dataset from the Food and Drug Administration (FDA) that would allow for plant-specific quality performance comparisons over time and across the pharmaceutical industry. "I sensed the unique opportunity to study the sustainability of quality advantage with this dataset," Siemsen says. Gray and Siemsen soon teamed up with the University of Illinois at Urbana-Champaign's Gopesh Anand to dig deeper.

Their suspicions were confirmed when they examined the data: strides made in quality performance were impressive, but tended to fall off—or decay—over time. As reported in their *Organization Science* article, "Decay, Shock, and Renewal: Operational Routines and Process Entropy in the Pharmaceutical Industry," FDA inspections prompted a renewal of attention towards process compliance-related routines. But, over time after the inspection, the tendency of all kinds of things to drift toward a state of high entropy takes over. Anand says, "People inevitably get complacent," and achievements in safety, quality, and time management fall off with less attentive implementation over time. Just as your new car become less reliable the longer it has not been inspected, the quality improvements of pharmaceutical plants also erode over time.

Siemsen, whose expertise lies in the fields of forecasting, operations strategy, product development, and project management, says he can think of three key takeaways for those who hope to see improvements in pharmaceutical company practices be sustained—and even refined—over time: "The implications for the FDA are quite clear," he says. "The longer it's been since a plant has been inspected, the more likely it needs an inspection. Similarly, there should be an inspection any time there's a plant merger." Siemsen says some of this "risk-based" inspection has been undertaken, but only as a pilot program within the FDA.



Discussing the work with the University of Illinois at Urbana-Champaign's press office, co-author Anand says the FDA doesn't need to be in every factory every week, but, "There's the sense that when you do things over and over again, you get better... But that's not the case. You can't assume that there's going to be stability... [or] consistent quality. Companies themselves can do a better job of internal inspections and oversight."

And that leads to Siemsen's third recommendation: "For those in the industry, I advise that you never rely on your quality capabilities to sustain themselves. Even if things look good, regularly perform internal renewals related to compliance and quality. Don't become complacent," he says. Internal renewals discussed in the paper include mock inspections involving high-level managers, periodic review of compliance-related measures, and frequent behavioral inspections. And for those in his own academic ranks, Siemsen recommends new avenues of research to improve policy, industry, and the safety and effectiveness of pharmaceuticals: "Explore drivers of quality sustainability," he says. "Our paper shows that quality naturally erodes over time, but some companies are better at keeping this in check. Why? What can they teach everyone else?" ■

About

Exchange, a publication from the Medical Industry Leadership Institute, features dialogue on medical industry research and application. The content is a summary of research from both academia and the medical industry, followed by commentary on the importance of the research and its application. Topics highlighted in the *Exchange* span all sectors of the medical industry and include commentary from leaders in the field, as well as researchers from the University of Minnesota and other academic institutions.

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Exchange—A dialogue on medical industry research and application

Commentary

*by **Richard Manning, PhD**, Partner, Bates White, LLC*

The article by Anand, Gray, and Siemsen covers an important and topical issue. Manufacturing quality in the pharmaceutical industry underlies concerns about patient safety, regulatory effectiveness, and even health care costs.

The salience of this issue is underscored by a recent report issued by the U.S. Government Accountability Office (GAO-04-339T, February 10, 2014) (GAO) that found a substantial increase in drug shortages in the U.S., rising from 154 total shortages in 2007 to 456 in 2012. A key cause of the shortages was supply disruption associated with quality problems in the manufacturing process (often correlated with FDA inspections). Hence, new research that identifies causes of quality erosion in drug manufacturing has the potential to make a meaningful contribution not only in the academic literature, but also in the real world, where businesses operate and patients live.

At one level, the key finding of the Anand study is not terribly surprising. That is, it seems fairly natural that people's attention to detail might wane as they gain experience and engage in a process time and time again. Though predictable, it is unfortunate that such inattention might take place in a critical enterprise such as the manufacturing of medicines—doubly so when such lapses put patients at risk.

The Anand study attempts to drill down to some of the key causes of quality degradation, an important threat to manufacturing quality, but there are certain important questions, including how to avoid such lapses, that the study is not equipped to answer. Further research would be most helpful.

For example, the GAO found that generic injectable drugs accounted for 44 percent of the 219 critical shortages identified. Since injected medicines typically require greater care in manufacturing, shipment, and storage than oral solid forms, it would be helpful to distinguish between types of products and types of manufacturers to help in focusing business and regulatory attention.

This study also finds that larger firms with multiple manufacturing locations tend to have less quality degradation than do single location manufacturers. But beyond that, it would be useful to know whether there is anything *specific* about generic manufacturers, given the cost competition and thin margins of that sector, that leads to increased entropy in manufacturing processes. It would also help to learn whether there are important differences between domestic generic manufacturers and those headquartered abroad. Here again, Anand does some limited exploration, but the results are similarly limited. The data at hand does not contain enough information to allow comparisons beyond the U.S. and Europe. This is particularly unfortunate at a time when manufacturing of medicines is growing rapidly (in Asia in particular) and when many newer medicines are of injectable form. The emergence of biosimilars in the U.S. will only exacerbate such concerns.

We simply need to know more about the underlying relationships among global competition, market structure, regulatory processes, and the continuing manufacture of a safe supply of new and established drugs and biologics. Studies like this are a step in the right direction. ■