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Blood Glucose Meter Accuracy Problems Acknowledged By FDA, Industry And Clinicians

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The Diabetes Technology Society sponsored a meeting last week entitled, "Do Currently Available Blood Glucose Monitors Meet Regulatory Standards?" The resounding answer from participants: No.

Clinicians, industry, academics and FDA agreed that certain 510(k)-cleared blood glucose meters do not perform at the regulatory standards for which they were cleared after they hit the market.

"The problem is that there are some blood glucose monitors on the market which perform less accurately than the standards would specify and it's these standards which led them to be approved," explained David Klonoff, a clinical professor of medicine at the University of California, San Francisco, in an interview.

FDA currently follows the International Organization for Standardization (ISO) 15197:2003, "Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus" when assessing blood glucose meter 510(k) pre-market applications. On May 15, ISO published a revised 15197:2013 standard, which has stricter accuracy guidelines for blood glucose meters, although FDA has yet to adopt it.

"After they're on the market, some monitors – we estimate 25 percent, but with tighter standards could be as much as 50 percent – do not, or are expected in the future to not, perform up to the standards which led to their approval," said Klonoff, who is also president of the Diabetes Technology Society, a nonprofit that promotes the development and use of technology for diabetes.

FDA previously indicated that it intends to tighten its standards for home-use blood glucose meters at a March 2010 public meeting. (See *"FDA Weighs Tighter Standards For Blood Glucose Meters At Public Meeting" – "The Gray Sheet," Mar. 22, 2010.*)

"We're concerned about this issue as well," said Katherine Serrano, diabetes branch chief in CDRH's Division of Chemistry and Toxicology Devices, at the meeting. "That's why we had the meeting in 2010; that's why we've been working to come up with criteria that are appropriate."

But she noted "it's not easy" for the agency to make these regulatory changes.

"We are under a regulatory system where the legal bar is substantial equivalence and there's a process for making changes that would allow us to more easily enforce these different changes in the standards. That is something that we are pursuing but it's not here yet," she said.

Precisely what steps FDA plans to take have not been disclosed, but there is an expectation in industry that regulatory standards will be heightened for glucose meters.

"It's pretty clear that the FDA wants to come out with something even stricter, at least at low glucose levels, but they haven't divulged what that would be," Alan Cariski, **LifeScan Inc.**'s VP, worldwide medical affairs, and medical safety officer, said in an interview.

But beyond tightening standards for these devices, stakeholders at the meeting agreed that there is a need to focus ways to ensure the devices already on the market meet the current standards.

Quality Costs Money

There are several factors that contribute to the poor performance of certain blood glucose meters once they hit the market, Klonoff explained.

He pointed out that diabetes test strips are biological products, and are particularly vulnerable to undergoing some change between approval and the time they hit the market.

He also pointed to the possibility that products are not shipped, handled and stored according to the manufacturer's specifications, and as a result the products may be exposed to environmental conditions, including extreme high or low temperatures, and humidity, that could degrade their performance.

Meeting participants argued that the majority of the poorly performing blood glucose meters are made by foreign manufacturers overseas, primarily based in Asia.

During the meeting, Ronald Brazg with the Rainer Clinical Research Center in Renton, Wash., presented his study, published in January in the Diabetes Technology Society's Journal of Diabetes Science and Technology. The study, sponsored by Roche Diagnostics Corp., compared Roche's *AccuChekAviva Plus* blood glucose meter with six other meters, four of which were made by companies in Taiwan and Korea, and found Roche was the only meter with readings that met the new ISO 15197:2013 standard.

LifeScan's Cariski said, "It's expected that the product would continue to have the same performance characteristics when it's on the market. In order to achieve that, you need all kinds of quality controls – lot-release testing, you have to be

very careful about your sourcing, you have to be very careful about your manufacturing tolerances."

Cutting corners on quality controls leads to "big savings in money," Cariski underscored. "We spend a lot of money on lot testing, and reporting [adverse events] to the FDA."

Abbott's Jared Watkin, VP, R&D at Abbott Diabetes Care Inc., made the same point.

"We certainly see this pattern of newly approved systems [tailing] off in performance as they roll out into the marketplace, and that frankly is because the cost of sustained quality is high. You have to put a lot of effort into it – from a process control perspective and an R&D perspective and a quality systems perspective."

LifeScan's global recall in March of its *OneTouchVerio IQ* blood glucose meters due to a software glitch is just one example of a cost-intensive quality control initiative. And the firm just recalled the systems in Saudi Arabia May 23. (See *"Regulatory News In Brief" – "The Gray Sheet," Apr. 1, 2013.*) As a result, Abbott tested their *FreeStyle InsuLinx* meters and recalled them due to the same software problem in April. (See *"Abbott Recalls* Freestyle InsuLinx *Glucose Meter Following Similar J&J Recall" – "The Gray Sheet," Apr. 22, 2013.*)

"I wonder whether any of these other manufacturers ... have a problem, and who knows because you either have to examine the software or the simpler way would be to test high glucose levels. But to my knowledge that hasn't been done," Cariski said.

FDA Foreign Inspections A Challenge

FDA says it is a challenge to conduct inspections of foreign manufacturing facilities. Unlike in the U.S. where inspections can be unannounced, FDA is required to announce inspections in some countries overseas.

"We have seen fraudulent data upon inspection. It's not common luckily, but it does happen, and it's very difficult to detect. Foreign manufacturer inspections are not unannounced in some countries, and so that actually also has an impact on how effective certain inspections can be," explained Courtney Lias, director of CDRH's Division of Chemistry and Toxicology Devices, at the meeting.

CDRH's Serrano added, "It's a real challenge for us to go and do inspections outside of the United States, particularly in Asia. We have done it, we continue to do it. Getting good data out of those inspections is a challenge which may be why you don't see the same data generated from an inspection. But it's something that we are also concerned about."

Seranno said FDA faces data integrity issues with certain blood glucose meter data as well.

"Manufacturers do sign a truthful and accuracy statement, but I can tell you that we've had many cases where the data seems a little too good and maybe not perfect, but it's sort of perfectly imperfect," she said.

"But we're in a tough spot because unless we actually go out on an inspection and find information showing that there was fraudulent activity going on, they signed a truthful and accuracy statement, we have data in front of us, and that is really what we have to make our decision off of."

Competitive Bidding To Make Things Worse?

The large glucose meter manufacturers argue that product quality issues are likely to be exacerbated by the nationwide competitive bidding program for mail-order diabetes supplies, which will set Medicare payment rates beginning July 1.

CMS announced the winning bid rates in January, adding up to an on-average 72 percent reduction in payments for mail-order glucose test strips. And under a recently passed legislation, the same supplies sold at retail will be subject to the same cuts. (See *"Medicare Durable Equipment Cuts Will Deepen In Next Round Of Competitive Bidding" – "The Gray Sheet," Feb. 4, 2013.*)

Companies worry that additional pricing pressures may force more firms to cut back on quality control measures.

"We're concerned that in the face of ongoing competitive pricing pressures some companies have compromised or will compromise their quality systems, and that operating with razor thin margins, they may not make the tough decisions to recall product[s] when the data so dictates," Cariski said at the meeting.

David Simmons, chief medical officer of Bayer Diabetes Care, further elaborated the point.

"CMS is about to drive a substantial change in the market dynamic, and the only characteristic that you have to have [for] quality [to] be in the competitive bidding is that you are an FDA-cleared device, which means that you can have performance at all ISO standards without any assurance of performance in the market space as we heard now," he said at the meeting.

"We are about to see a dramatic increase in the probability that our patients are going to be provided – purely on price – with meters that we do know are not going to perform at the standards that we'd like to see them perform."

The large firms have been pressing CMS to move more slowly on competitive bidding for diabetes supplies, concerned about a drop in quality and a loss of market share. (See *"Industry Urges Delay In Nationwide Bidding For Mail-Order Diabetes Supplies" – "The Gray Sheet," Sep. 6, 2010.*)

The meeting did not conclude with a clear-cut list of action items, except for pledges of continued collaboration.

"The Diabetes Technology Society plans to work with the regulatory community, the manufacturing community, the academic community, and the clinical community to find a solution to this problem which we've identified today," Klonoff said.