

DIABETES CLOSE UP

Diabetes Close Up
April 2005, No. 46
Continuous Monitoring Update ~ MS Unplugged

The Shorter Version

In this issue - diabetes/obesity news of note:

- **Continuous monitoring update**
- **Ready, Set, TIVO dLife**
- **Oral insulin approved in ... Ecuador?**
- **Bill Clinton's getting in on childhood obesity prevention – hurrah!**
- **Morgan Stanley's Unplugged conference ~ the setting for interesting M&A fodder**
- **Conference update – key current upcoming meeting watch**
- **Annual report watch – ABT, AMLN, BDX, and JNJ**
- **Literature watch: *DOC News* on the new public enemy**
- **Earnings update – blood glucose monitoring results for C1Q05**
- **Glucose patent update, early 2005**

1. **Continuous is the word, is the word, is the word / Conference issue coming up:** There is SO much attention on next-generation glucose monitoring right now, and there's sure to be even more to come as the importance of improving glucose levels and glycemic variability becomes even more understood. We applaud it, as longtime readers know. Our next issue will focus on recent conferences, including last month's meeting on this topic and insulin delivery, organized by Dr. David Klonoff in San Francisco, where continuous monitoring was a major focus. In the meantime, we direct you to a volume published on continuous monitoring by the New England Healthcare Institute. NEHI really nailed the major challenges associated with continuous monitoring. Download the report at www.nehi.net. Other key conferences that will be highlighted next time include the IV International Assisi Symposium – New Technologies for Insulin Replacement, Diabetes UK in Glasgow the 1st International Congress on Pre-Diabetes and Metabolic Disease in Berlin, and the International Pancreas and Islet Transplantation Association meeting in Geneva.
2. **Ready, Ready, Set, TIVO ~ dLife!** Last month, we told you about dLife, the new talk show on diabetes aired Sundays at 7 pm EST on CNBC. Some recent shows have been outstanding, such as one that featured former ADA President Dr. Francine Kaufman on the twin epidemics of diabetes and obesity. See the March issue of DCU for our review of her compelling volume *Diabesity: The Obesity-Diabetes Epidemic That Threatens America – and What We Must Do To Stop It*, published in March by Bantam. In our view it should be the newest favor given out at cocktail parties. Everyone should read and internalize it.

We see diabetes going more direct-to-consumer than ever, and we applaud the work on this show, which we believe represents outstanding outreach to patients and families. Reimbursement for diabetes education in the U.S. is a significant problem and must be addressed for care improvements to really make a difference. In the meantime, we believe dLife can start to help educate patients and families and probably even some healthcare providers assuming enough experts continue to be scheduled – the clinical advisory board is very impressive. Importantly, the show is not appealing just to hyper-intensive and motivated patients, but also (perhaps even more so) to patients who have historically been decidedly less engaged. So think mass market diabetes; everyone needs to learn, and we think education through means like dLife ultimately have the power to help improve outcomes—all good.

3. **Morgan Stanley Unplugged:** There are some really interesting conversations that take place at investment conferences, though it's probably fair to say most of them are in the hallways. Sometimes, the main events are

of great interest as well, however, and that was definitely the case for with Morgan Stanley's recent Unplugged conference. That's because the sessions are basically all breakout sessions, and when you have ones run as well as the ones by expert griller and master interlocutor (and longtime Morgan Stanley Managing Director) Glenn Reicin, there's bound to be big interest. He keeps the pace fast, asks tough and/or very searching questions, and barely offers time to breath – this contributes to wonderfully interesting interviews, as was the case of Mike Dormer, J&J's Worldwide Chairman of Medical Devices. When Glenn casually asked about the global strategy for diabetes (“When we will find more about that?”), we were all ears ...

4. **Glucose Patent Update:** This is an occasional column written by patent experts Russ Potts and D. Bommi Bommannan – see inside the longer version for more details on recent patents related to glucose monitoring.

The Longer Version

- 1. Continuous monitoring update:** So what was *most* interesting to us about this meeting in Italy recently – the IV International Assisi Symposium, held in collaboration with the International Study Group on Innovative Insulin Delivery Devices – was that it seemed that Medtronic’s Guardian RT real-time sensor had received regulatory approval in Europe. We thought it interesting that we hadn’t heard that previously, but if one does a search on the Medtronic website, after a few clicks one comes up with the Medtronic UK website that suggests it is approved: <http://www.medtronic.co.uk/UK/health/diabetes/guardianrt.html> We have received conflicting reports on this front, however. Medtronic did say at the meeting it expects US approval for the sensor-augmented pump within the next 12-18 months, presumably for an adjunctive label, following EU approval, but it actually isn’t clear whether there is approval yet, despite the website. Some confusion may exist because approval in Europe seems to be mainly focused on safety, not efficacy – there is no reimbursement word yet. We’ll stay tuned on this front and keep you posted. Also on the continuous front, the NEHI report we refer to in the shorter version is an analysis that examines the growing need for continuous monitoring technology, the value of the technology, and the barriers that could prevent (and have already prevented, in first generation devices) timely adoption. The barriers are very well articulated and focus on regulatory (label), reimbursement, and education challenges. Ultimately, NEHI serves as a valuable call to action to industry to pursue standards and evidence guideline creation, reimbursement improvement, and proper education, all to the end that the devices are rapidly adopted. To read the report in full, click on http://www.nehi.net/CMS/admin/cms/_uploads/docs/NEHI_%20CGM_Report_2005.pdf. The executive summary is available at http://www.nehi.net/CMS/admin/cms/_uploads/docs/CGM_Exec.pdf.

– by Melissa P. Ford and Kelly L. Close

- 2. Ready, Set, TIVO ~ dLife!** Last month, we told you about dLife, the new talk show on diabetes aired Sundays at 7 pm EST on CNBC. Some recent shows have been outstanding, such as one that featured former ADA President Dr. Francine Kaufman on the twin epidemics of diabetes and obesity. See the March issue of DCU for our review of her compelling volume *Diabesity: The Obesity-Diabetes Epidemic That Threatens America – and What We Must Do To Stop It*, published in March by Bantam. Upcoming episodes include interviews with thought-leader Dr. Steve Edelman on new insulin developments, Dr. Aaron Kowalski of the JDRF on work the organization has recently begun on the continuous monitoring/artificial pancreas front, and noted R.Ph. Keith Campbell discussing new diabetes product developments.

The approach to diabetes is going more direct-to-consumer than ever, and we applaud the work on this show, which we see as outstanding outreach to patients and families. Reimbursement for diabetes education in the U.S. is sub-optimal at best and must be separately addressed, but in the meantime, we believe dLife can help educate patients and families in a creative and appealing way. Importantly, the show is not appealing just to hyper-intensive and motivated patients, but also to patients who have historically been decidedly less engaged. This is interesting; personally we love anything that can improve A1Cs from 7.5 to 6.5 or 7 to 6, but where the country can really use more help is getting average A1Cs from 12 to 10 or from 10 to 8. It is these patients that are experiencing all the complications and that are really increasing the dollars spent. While there is sometimes lots of focus on drug spending, well, you all know that \$92 billion in total direct spending on patients with diabetes – less than 20 percent is estimated to go toward drugs, while upwards of 40 percent goes just toward patients that are hospitalized – doesn’t it seem like we should focus more on keeping patients out of the hospital through more aggressive therapies?

So, absolutely, it’s great to want everyone at goal or better (below 6.5 - 7.0% A1C), but if the average A1C is 9.3, it’s more important to focus first on how to keep the patient out of the hospital and how to achieve the first 1.0 drop – now *that’s* how microvascular and macrovascular complications will be staved off. These patients have the worst outlooks and need the most help, and, too, these are the ones that are costing the healthcare system the most – so yes, the creation of a TV show for them is brilliant! We met with Howard Steinberg, the founder and executive producer, about a year ago (he has type 1, his A1C is 5.4, and he is amazing at making things happen) and we’re really moved by what he’s done in 12 months. Think mass market diabetes; everyone needs to learn, and we think education through means like dLife ultimately have the power to help improve outcomes—all good.

To date, ratings and audience metrics for dLife have been remarkably strong, particularly for such a targeted show: an estimated 300,000-plus weekly viewers tune in with an average 1.9 viewers per household. This last stat is significant because it reflects the importance of family and caregivers sharing the disease management. To boot, there has been impressive awareness of dLife among households with diabetes—over 10% after just five shows. As always, seeing the ads has been fun. We think the show will prompt some increases in DTC TV ad budgets among manufacturers, and we'll be on the lookout for improvement on this front. To date, we still think Roche's are the best. If you miss them on dLife, you might be able to check them out at ADA. Take a look even if (*especially* if) you're a competitor; they're a good window inside what it's like to be a patient with diabetes.

– by *Melissa P. Ford and Kelly L. Close*

- 3. Generex's Oralin and Ecuador:** It appears that Oralin, oral insulin, made by Generex, has been approved in, um, Ecuador, according to a release on the company's website. Meanwhile, it is not yet in Phase 3 in the US. This oral insulin formulation is said to be delivered into the mouth via a "Rapidmist" device, where it's then absorbed into the bloodstream. We will look out for more on this at ADA. This press release was a surprise and we don't know much about label, dosing specificity, safety, etc. We suspect the market for patients with diabetes in Ecuador is rather small, but we're still interesting in patient feedback. Oral insulin was used in a major diabetes prevention trial years back – it did not show efficacy, but one never knows if the dose was optimized. That said, there is surely some major skepticism over this release. I have to admit that we haven't studied the Ecuadorian diabetes market in any depth.

– by *Kelly L. Close*

- 4. Bill Clinton and the AHA/Childhood Obesity Prevention Initiative:** You may have seen the headlines about Bill Clinton joining the AHA force to speak out against childhood obesity. I saw this and was mostly skeptical, because these prevention schemes seem mostly blue-sky, but for this one, the approach and early execution have been compelling. First of all, Clinton himself is obviously very engaged by the problem and children were responding to him so naturally in the press conference – you couldn't invent some of this stuff, it was so wonderful! Second, Clinton's fellow spokespeople are also very persuasive, in particular, Arkansas Governor Mike Huckabee and AHA President-Elect Robert Eckel. It's all very inspired and seems quite genuine. To start the original press conference, Huckabee told some of his own story, which includes losing 110 pounds over the last two years because his doctor told him if he didn't change his behavior, he was in the last decade of his life. In March, the governor ran his first marathon in Little Rock! This was obviously not an easy path and I respect people who can make this change. He then went on to discuss problems with children with type 2 diabetes, specifically that if they have type 2 in their pre-teens, they'll have vision problems in their 20s, heart attacks in their 30s, dialysis in their 40s, and death in their 50s. Some fear seemed to permeate the room – is fear the best teacher? It's unclear, but other education hasn't been so effective and we applaud straight talk.

Tatiana Disa of PS128 in New York introduced "William Jefferson Clinton, the 42nd President of the United States" with a lot of entertaining pomp and circumstance – the kids were amazing to watch. She reminded us that Clinton warned us of obesity during his presidency, which I must say, I don't remember, but his talk was terrific. Clinton rose, thanked Tatiana, and pointed to Huckabee, "*Half the size of when they met*" (in an aside, Clinton noted that he had always wanted to shrink the ranks of Republicans but hadn't realized how much that could happen until Huckabee, prompting truly raucous laughter) and explained the strides ("*astounding work*") that Governor Huckabee had made in Arkansas – he's having the BMI of every child measured and sending it home like a report card and is railing against the makers of sugar and fatty foods, attempting to work against the vending machine lobby. Rather than shock us with a million scary stats, Clinton used facts more selectively, reminding us, for example, that fried potatoes make up half (half!) the vegetables eaten of children between 2 and 19 and that children are getting no more exercise today than 20 years ago even though the benefits are very clear. He noted that although the overall rate of overweight/obese in the US among children was 16%, in some southern states it is as high as 25%, especially in lower-income areas. They clearly understand there is a real link between income and obesity, which is critical. They seem to be going after a number of groups in a pretty strident way – we'll see, but they aren't mincing so many words, which is a plus. More thoughts from his talk –

while these may not seem groundbreaking, we think if Clinton were seriously involved, he could bolster efforts in an important way:

- Restaurants, chains, and food producers should create healthier alternatives
- Schools should promote better food and exercise – they say they will work with food and sporting goods companies and seemed to be trying to be critical but not scare them off completely – they also noted flat out that schools were doing a very poor job of promoting exercise, which should be.
- They like grassroots campaigns and also said they would go after enemies like food companies
- They would like to help bolster a market for healthier eating and lifestyles – unclear how that would happen because they acknowledged, thankfully, that parents are working longer hours and that there is not a good end in sight. “*Half the US food dollar is spent eating out ...we must give better choices.*”

Clinton closed by quantifying his goal – to increase prevention of childhood obesity, he said, he would like the average child to drop 45 calories a day from food intake, which he said would prompt a drop of two pounds per year, which could make children 20 pounds lighter when they graduated. “I want all children to live to 90,” he said. He expressed profound gratitude to the AHA and to Huckabee.

Clinton appears to be in very good shape following his heart surgery and having lost 15 – 20 pounds. He was very overweight as a young kid, he said – 210 pounds at 15. But he said that from 1970 to 1995, he ran 25 miles per week. He now weighs what he weighed when he finished high school (190) but he has struggled with weight throughout his life.

Clinton said he knew he would have (and this is the main place he gets low marks due to poor prepping) developed “adult onset” diabetes (that term has sort of been banned for years but still gets used occasionally, though isn’t so relevant due to all the children with type 2). He noted that a substantial number of children get type 2 due to eating and exercise, following up by saying that it’s all about what children eat, how it is prepared, and how it is offered. When a member of the media asked how much it would cost, Clinton didn’t respond directly, but said with gumption, “We will find the money to do it because it needs to be done.” If Clinton really could get behind this and if he could work together with Dr. Fran Kaufman (*Diabetes* author), we’d be in terrific shape! We have sent an e-mail to the AHA about this and hope it happens. As a natural advocate, Clinton could use his authority and stature to make some things happen. Here’s hoping ...

AHA President-Elect Eckel followed up by saying that children should have a minimum of 60 minutes a day working out, that the portion sizes should be made smaller, that the preparations should improve (no more frying everything as they do in the South), that they should actively promote healthier lifestyles, and impressively, focus on both overweight and obese children and also children who are not yet overweight. He also stressed that parents must actively participate and implied those that don’t are quite pathetic.

There does seem to be real thought and money put into this campaign, although we haven’t yet found out the budget (and probably will continue to have a tough time doing so). The new initiative, launched at an event in New York City, will target several areas that the group hopes will spark change and reverse the rising rates of childhood obesity in the United States. This includes, as shown on the website:

- Working with the food and restaurant industry to improve the quality and portion size of food products and to develop marketing and promotion strategies that support environmental change within the industry.
- Increasing physical activity and improving nutrition in schools across the US.
- Exploring opportunities to work with the media to promote positive behaviors.
- Creating a campaign to engage kids – particularly those from ages 9 to 13 – to take steps to make healthy lifestyle choices.
- Creating tools and providing opportunities for healthcare providers to better recognize, prevent and treat obesity in children.
- Providing tools and information to parents to help them incorporate heart-healthy activities into family routines.

Again, to start I was mostly skeptical, but I also downloaded the statistical sourcebook (link below) – some impressive work has been done. Then I watched the video online that I wrote about above. It’s really inspiring. I like how the statistical sourcebook begins: “*It’s gut-check time ...*” There’s not a whole lot of getting away from what that means. Overall, the joint goal of the Clinton Foundation–American Heart Association partnership is “to stop the increasing prevalence of childhood obesity in the United States by 2010 by fostering an environment that helps all kids pursue a healthy lifestyle.” I couldn’t imagine a better partner in this fight than President Clinton. The link to the statistical sourcebook is <http://www.americanheart.org/downloadable/heart/1114880987205NationAtRisk.pdf>, as is the video of the press conference. Some stats of notes from the sourcebook:

- 12% of the US healthcare budget goes to obesity, according to the World Bank
- The percentage of overweight children and teens in the US is double-digits for all age groups except males age 2-5, which teeter at 9.9%. 27% of Mexican males age 6-11 are obese and 24% of non-Hispanic black females aged 12-19 are overweight or obese. Overall, for all children and teens in the US, 16% are overweight or obese.
- Twice as many children and three times as many teens in the US are overweight or obese vs. 25 years ago. Even preschoolers aren’t immune – the prevalence of overweight/obese among the two-to-five-year-old-set now exceeds 10%, up from 7% in 1994, an increase of over 40%.
- Of course adults are the worst – 65% are overweight or obese in the US and 30% are obese. 49% of non-Hispanic black females are considered obese, according to *JAMA*, 2004 (Hedley, et. al.)
- Socioeconomic status does not appear to affect obesity among men, but women of a lower socioeconomic status are 50% more likely to be obese than those of high socioeconomic status.
- Low poverty areas compared to high poverty areas have a 50% increase in overall outdoor places to engage in physical activity.
- Those with a BMI of 35 or more have a six times greater risk of obesity than someone with a BMI of less than 25 but “only” a 1.67 times greater risk of heart disease. Even a BMI of 25-30 carries with it a 2.4x greater risk of diabetes and a 1.4x greater risk of heart disease.
- You’ve all heard that stat from *JAMA* two years ago (Narayan, 2003; 290:1884-90) about children born in 2000 having a one in three times risk of diabetes. Turns out that 45% of Hispanic boys and 53% of Hispanic girls are likely to develop diabetes at some point in their lives and 49% and 40%, respectively, of African American girls and boys.

We’ll be watching next steps closely!

– by Kelly L. Close

5. Morgan Stanley Unplugged: Before reviewing first quarter results of note, below we note that Morgan Stanley recently had its annual Unplugged conference – this is where company management are essentially interviewed rather than giving presentations with limited Q&A time. I can’t imagine that companies would want to speak to Glenn Reicin of Morgan Stanley without some *serious* prepping since his questions are never particularly easy – as I sat and listened, I realized once again the guys gives nothing for free. That’s part of what makes sessions these so interesting and I’m sure part of what also earns him such all-around respect.

- **J&J on Diabetes:** Of interest. Glenn interviewed Mike Dormer, Worldwide Chairman of Medical Devices for J&J.
 - Glenn noted to Mike what a major opportunity diabetes is for a company like J&J and wondered how J&J would expand its presence. Indeed, J&J doesn’t speak much about diabetes outside LifeScan, but of course it’s true that the company *could* address diabetes more broadly on the pharma side, on the biotech side, and/or on the medical device side (in addition to LifeScan and its bariatric surgery business – it bought Obtech in 2002).
 - J&J doesn’t speak often about its earlier-stage pharma or medical device pipeline, but they have noted historically they are working on a DPP-IV inhibitor (Phase 2) and undoubtedly other drugs as well.
 - Mike agreed with Glenn that diabetes is a major opportunity and then, it was like the best kind of tennis match! You know where your head just goes back and forth and back and forth and quick as anything, the shot is over, but you saw something good, i.e., some great baseline shots, good volleys here and there, some passing shots. Glenn quickly jumped on Mike’s broad characterization of this great opportunity (diabetes) and asked quickly whether he

meant that on the drug or device side. Mike indicated that both sides were outstanding opportunities and that indeed, on the device side, the holy grail was the closed loop. Glenn then asked outright when some visibility on the strategy would emerge, and Mike indicated the answer depended on the age-old question, buy or build (“*that depends on whether we grow organically or through acquisition*”). Mike also pointed out that J&J were net divestors from 2000 – 2004. Will that continue, will it not ... ?

- **Abbott** didn’t include any commentary on diabetes at Unplugged.
- **BD discussed diabetes a bit**, noting that it would like to get more traction on the diabetes side of the business. Glenn asked when they would own their manufacturing: “*Longer-term, we must own our own destiny,*” was the answer there. Five years forward, it was articulated by CFO John Considine and team, the technologies used by patient would be different. When asked by Glenn when they will articulate a broader diabetes strategy, they said 18-24 months from now. They referred to continuous and in-dwelling sensors and then when asked if they would bootstrap, the talking stopped ... “*I can’t talk about it ...*”

– by Kelly L. Close

6. Conferences update – key current upcoming meeting watch: In mid-April there was a lot of activity in the diabetes/obesity arena and notably, we’re now in conference season in earnest. We sent or will send correspondents to most of the following conferences and will provide high level perspective on information presented in the next issue of DCU, which will be a conference special.

- The 1st International Congress on Prediabetes and the Metabolic Syndrome – Berlin, April 13-16, www.kenes.com/prediabetes/
- The Clinical Diabetes Technology Meeting – San Francisco, April 15-16, www.clinicaldiabetestechology.org
- Diabetes UK, April 20-22, 2005 <http://www.diabetes.org.uk/apc/index.html>
- IV International Symposium – New Technologies for Insulin Replacement, April 28-May 2, Assisi, Italy
- The International Pancreas and Islet Cell Transplantation Association Congress, May 4-7, Geneva <http://www.ipita2005.org>
- The Pediatric Academic Societies, May 14-17, Washington DC.
- AACE takes place May 18-20 in Washington. There will be a LOT on obesity at this meeting. Of note on the schedule are sessions led by
 - Dr. Robert Misbin of the FDA on improving drug trials for type 2 patients
 - Dr Lois Jovanovic on diabetes in pregnancy
 - Dr. Judith Korner on regulation of appetite and strategies for pharmacologic intervention
 - Dr. James Sowers (moderated by Dr. Daniel Einhorn) on hypertension and diabetes
 - Dr. Christie Ballantyne (moderated by Dr. Paul Jellinger) on new biomarkers for vascular disease
 - Dr. Noel Williams on surgical management of obesity
 - Dr. Pierre De Meyts on the science behind insulin analogs
 - A slew of interesting symposia
- Endocrine Society takes place in San Diego, June 4-7. www.endo-society.org - look for lots on obesity here, including data on Amylin’s AC137 and undoubtedly on Sanofi-Aventis’ Rimonabant.
- Don’t forget to register for ADA – San Diego, June 9-13, www.diabetes.org. The program came out; recently and here too, obesity – and hypoglycemia – are receiving lots of attention. Indeed, the entire program looks to be of interest – more on drugs than devices - and we’ve also just received the first set of in-depth symposia details – on June 10, sponsored by Sanofi-Aventis, “Strategies to Achieving Target Glycemic Control” chaired by Dr. Jay Skyler, who will speak on modern basal/bolus therapy, followed by Dr. Bruce Bode on enhanced technology for achieving glycemic targets, followed by Dr. Camillo Ricordi on islet replacement therapy. Very interesting subject choices for S-A- we’ll be following closely.

– by Melissa P. Ford and Kelly L. Close

7. Annual report watch

This is the time of year that annual reports start coming out for most public (and some private)

companies. We point to news on several. 1) In terms of the Big Cap companies, it is so interesting to watch, year to year, what the incremental relative changes are in terms of relative diabetes/obesity focus. 2) In terms of the small- and mid-cap size companies, the same thing is true – what’s also great here is that there are more and more pure-play public companies with a major focus on diabetes.

- **Abbott’s new annual report is out** – hipster diabetic teen Katrina Donnell graces the cover, giving Abbott Diabetes Care nice visibility. She reminds me a little of the people featured in the great J&J LifeScan advertising campaign from a few years ago, Live Life Without Limits, and also of the “real life” PWD (patients with diabetes) featured in Roche’s Compact TV commercials, especially the teens, which we wrote about a couple of issues back. Great to see. In the letter to shareholders and in the annual itself, excitement is expressed over the future of Abbott Diabetes Care, and in continuous monitoring in particular. It’s noted that ADC sales are expected to exceed \$1.0 billion in 2004, a real milestone.
- **Amylin’s report is also very interesting this year** – once again. Someone said to me recently, in so many words, so what is this post-prandial focus across the industry that I’m starting to hear more about, why is it important? Anyone who has that question should look at page 17 of the annual report and this Symlin data – you can find it on the company website. *This* is why we think people will take the drug. Another good page is page 23, where we see the 82-week (n=393) completer population weight and A1C data. We can just imagine what the scientists thought when they saw this – it’s exactly what one would hope for, but could one expect data this good at 82 weeks, where A1C improvement is sustained and/or that weight loss continues to increase? We’ll be eager to see more data at ADA, which is in Amylin’s hometown of San Diego, starting June 10.
- **BD also features a patient with diabetes on its cover**, yet another cool looking hipster young woman who is probably listening to Beyoncé on her iPod in the picture. The report features prominently products of note for PWD, including the BD Ultra-Fine III Mini Pen Needle, the shortest needle on the block (in the world, we mean), the BD Ultra-Fine II Short Needle Insulin Syringe (these short needles are considerably less daunting than the older syringes used to be), and the BD Ultra-Fine 33 lancets, which are the best lancets out there by a million miles in our option (they really barely hurt). One of the sidebars starts out by noting that worldwide, there are more than 180 million people with diabetes, including 400,000 children – actually, there are 400,000 children with diabetes in the US alone, we think. The report goes on to highlight the combined blood glucose monitoring and insulin delivery products put together by Medtronic and BD and to note that BD is well positioned to link data management to insulin delivery and glucose monitoring. The report also notes that BD has the ultimate goal of helping find a cure. We have no idea of content, but imagine there must be some very interesting discussions ongoing there. Finally, we can see a stronger DTC focus than in past years – BD notes its work with Gary Hall to close out the section – that was a real marketing win to bring over the type 1 Olympic champion swimmer.

– by Kelly L. Close

8. **Literature watch: DOC News on the new public enemy.** This new diabetes publication, aimed at PCPs, is really well done. I love it perhaps most of all because you can read in one sitting and feel like you’ve really learned—very diverse (Diabetes, Obesity, CVD disease) <http://docnews.diabetesjournals.org/current.dtl> The *really* good piece in the May issue is about the new public enemy #1, the hospital administrator. You can say *that* for sure! We attended a meeting described in this piece, in New York, in January – a physician challenge meeting, which was packed – the desire for this learning is significant from healthcare providers and the place was nearly SRO. Despite all the evidence in favor of considerably better in-patient blood glucose control, it seems that the administrators are the ones that need to be swayed. There are clear logistical, administrative, and political challenges representing barriers to improving the inpatient side: *“Ironically, hospitals have a greater incentive to treat the devastating complications of diabetes than to implement programs that help prevent many of the problems we all treat on a daily basis. This to me is the heart of the apparent impasse and the overall reason diabetes care in the United States is so poor—despite the fact that most of these complications could be avoided or postponed.”* There was so much enthusiasm at last year’s meetings to addressing these problems – here’s hoping that the administrators don’t win out – we mean, lose out.

9. Earnings update - Abbott, Roche, J&J and BD have reported C1Q05 results over the last month.

- **J&J had another extremely impressive quarter.** Sales reached \$501 million in the US, up 25% (23% excluding FX), versus \$400 million a year ago. This quarter represents the first time quarterly sales exceeded half a billion. US sales rose 24% to \$272 million, and international sales rose 26% (20% excluding FX) to \$229 million.
- **Abbott reported sales of \$247 million for the first quarter,** \$125 million in the US, up 139%, and \$122 internationally, up 36%. Management mentioned on the call that ADC is up two market share points versus a year ago and that there was good news on the United Healthcare formulary, where Abbott now has preferred status (13 million covered lives, 200,000-300,000 patients with diabetes). The company is leveraging international infrastructure in expanding the Mini (Flash) brand, which is now available in most major countries. The Navigator continuous monitoring program is expected to launch in 2006.
- **Roche diabetes results are tricky to compare this quarter** because they have moved professional glucose (the Hospital “Inform” franchise) from the diabetes care division to near-patient testing. Adjusted figures indicate that the area grew 4% in local currency, 2% excluding FX - but excluding infusion systems (pumps, whose worldwide sales fell 19% year over year), blood glucose monitoring grew 7%. Roche discussed four new products: 1) Aviva, the new “Advantage” (5 second test, 0.6 µL blood), 2) Multiclix, a new lancing device (over 80,000 sold in Germany from November to February); 3) Accu-Chek Spirit pump – this just received 510K approval in the US – overseas, over 1000 demo pumps have been placed, and over 500 patients are using the pump, with “excellent patient feedback” quote unquote, though we don't think this is such a competitive pump, 4) Accu-Chek CompactPlus (“anytime, anywhere” – this is the product family where Roche is spending a lot on DTC and seeing good success).
 - Globally, Advantage sales fell 8%. Active and Compact results grew 4% and 23%, respectively, while pump sales fell 19% (25% in the US). We hadn't realized pump sales overseas were so weak, though Roche has three strikes against it with its pumps off the market in the US, with other smart pumps remaining ahead on the feature front, and with competitive pump companies moving in more aggressively. We don't think this will improve unless/until the Roche pumps improve from a product offering perspective. Even the new pump, the Spirit, is not compelling in terms of features from our perspective. We saw this pump in Singapore in November at ISPAD and recently at Diabetes UK.
 - Interestingly, Roche said that the infusion area was weak due to its pump ban in the US, and Heino von Prondzynski, the CEO of diagnostics, noted, aloud, on the conference call, “*The FDA has received all materials... some time [ago]... I personally am getting a little bit angry...*” He sounded literally quite annoyed. A number of company—both big and small—execs have gone public with their irritation at the FDA lately— an intriguing pattern?
 - Roche noted that testing penetration is increasing due to rising insulin use, that the epidemic is garnering increased attention by stakeholders in healthcare, and developing markets, such as China and India, are providing substantial growth. On Aviva, they noted capacity for 2 million meters/year; they expect 1.5 billion Swiss francs in sales. The company said it would launch an A1C analyzer mid-year.
 - Roche is having an analyst meeting for diagnostics on May 17th, where diabetes will be featured.
- **BD reported \$17 million in blood glucose revenue,** consistent with expectations. Management notes the company is on track for \$75 million in blood glucose revenue for the year.
 - Three general components of growth were cited - 1) direct to consumer; 2) growth stemming from Medtronic relationship; 3) DME. They said the first two would be bigger growth drivers going forward, and DME would be less. We've seen them do more DTC work of late, for example, they advertise on dLife every Sunday evening in the US. While they didn't create these commercials, they are certainly investing more here than at the start, when they hadn't emphasized DTC investment as much.
 - Another area of growth cited was international: BD management is seeing solid sales in Canada where they launched earlier this year; too, the company had its first European launch recently, in Germany.
 - On the financial front, BD acknowledged that they still had heavy spending on meter promotions but implied strip pull through was improving. Likely, they are helped by having some very profitable patients in terms of pumpers, who typically test more than other users. Last, management noted that their expectation of a net contribution to BD from blood glucose monitoring of \$7 million.

– by Sara S. Dauber and Kelly L. Close

10. Glucose Patent Update; #2: 1Q05¹

A search of US, European and World patents and applications relevant to glucose monitoring (using proprietary search strategies) yielded more than 110 citations for February and March 2005. The citations are shown in Appendix 1. These citations were sorted into three categories:

- those using noninvasive or minimally invasive techniques (N/M) – 25% of citations:
- those using subcutaneous implants for continuous monitoring (S/C) – 40% of citations; and
- those using blood or other bodily fluids, such as interstitial fluids (B/F) – 35% of citations.

We have selected several interesting patents from February and March 2005 and have summarized them below. Note that published claims in an application could undergo significant changes before they issue in a patent. See our broader list in Appendix 1.

- **US 20050056552**

Peter Simpson and Paul Goode

Increasing bias for oxygen production in an electrode system

Implanted glucose sensors often perform poorly due to low tissue oxygen concentration relative to glucose. In these situations, oxygen, not glucose, becomes rate-limiting. To overcome this problem, many sensors use membranes to limit glucose diffusion (but not oxygen) to the electrode surface. This patent application uses the novel concept of generating oxygen from water *in situ* by an electrochemical reaction

Claim 1: An electrochemical sensor for determining a presence or a concentration of an analyte in a fluid, the sensor comprising: a working electrode comprising a conductive material; and a reference electrode comprising a conductive material, wherein the sensor is configured such that a bias potential can be applied between the working electrode and the reference electrode at a level such that the working electrode measures the concentration of the analyte and produces oxygen in a reaction with water or another electroactive species in the fluid.

- **US 20050054909**

James Petisce et al.

Oxygen enhancing membrane systems for implantable devices

As described above, many sensors use membranes to limit glucose diffusion (but not oxygen) to the electrode surface. This patent application describes one such membrane system.

Claim 1: An electrochemical sensor for determining a presence or a concentration of an analyte in a fluid, the sensor comprising: a membrane system comprising an enzyme domain comprising an enzyme that reacts with the analyte in the fluid as it passes through the enzyme domain; and a working electrode comprising a conductive material, wherein the working electrode is configured to measure a product of a reaction of the enzyme with the analyte, wherein the membrane system comprises a polymer material with a high oxygen solubility.

- **US 6873268**

Ronald Lebel et al.

Microprocessor controlled ambulatory medical apparatus with hand held communication device

This Medtronic-Minimed patent claims priority to an application filed on January 21, 2000 and contains claims related to a method of delivering drugs using an implantable medical device that is controlled by an external communication device. Although the focus appears to be on insulin delivery, the applicants clearly intend to cover the delivery of other drugs as well.

¹ See March, 2005 DCU for earlier 1Q05 segment.

Claim 1. A method of delivering a medium to a patient employing a medical system having an ambulatory medical device (MD) for providing treatment to a body of a patient or to monitor a selected state of the patient's body, and a communication device (CD) for sending messages to or receiving messages from the MD, the method comprising:

- containing a flowable medium in a reservoir of the MD; and*
- transferring at least a portion of the flowable medium from the reservoir to the patient with a pumping mechanism by:*
- programming the communication device with at least two quantities relating to drug delivery; and*
- configuring the medical device to simultaneously deliver a drug based on the combined amounts associated with the at least two quantities.*

This list and review were produced by Russ Potts, PhD of Russ Potts Consulting, LLC (russ@vospotts.org) and D. Bommi Bommannan, PhD, JD of MaxVal Group, Inc (bommi@maxvalgroup.com).

Appendix 1: Glucose Patent Update Detail

Patents and applications in glucose monitoring during February and March, 2005.

Note the absence of an Assignee means that there was none assigned.

Publication	Title	Assignee
<u>US20050043602A1</u>	Method of monitoring glucose level	A.D. Integrity Applications Ltd.
<u>WO05017642A2</u>	A METHOD OF MONITORING GLUCOSE LEVEL	A.D. INTEGRITY APPLICATIONS LTD.
<u>US6863800</u>	Electrochemical biosensor strip for analysis of liquid samples	Abbott Laboratories
<u>WO05015163A2</u>	APPARTUS AND METHOD FOR MEASURING BIOLOGIC PARAMETERS	ABREU, Marcio, Marc, Aurelio, Martins
<u>WO05022143A2</u>	METHOD AND APPARATUS FOR ASSAY OF ELECTROCHEMICAL PROPERTIES	AGAMATRIX Inc.
<u>EP1503203A1</u>	INGREDIENT CONCENTRATION MEASUREMENT METHOD AND DEVICE	ARKRAY, Inc.
<u>EP1111386B1</u>	Test strip for the assay of an analyte in a liquid sample	Bayer Corporation
<u>US6859738</u>	Method and system for predicting initial analyte values in stored samples	Becton, Dickinson and Company
<u>US6855556</u>	Binding protein as biosensors	Becton, Dickinson and Company
<u>WO05024397A2</u>	SAMPLING INSTRUMENT	BEN-GURION UNIVERSITY OF THE NEGEV RESEARCH AND DEVELOPMENT AUTHORITY
<u>US20050029097A1</u>	Electrochemical sensor strip with low porosity screen	BT Medical Corp.
<u>WO05019803A2</u>	MEASURING ANALYTES FROM AN ELECTROMAGNETIC SPECTRUM USING A WAVELENGTH ROUTER	C8
<u>WO05029070A1</u>	BIOSENSORS HAVING REDUCED HAEMOCRIT EFFECT	CAMBRIDGE SENSORS LIMITED
<u>US20050056551A1</u>	Electrochemical detection of analytes	Cranfield University
<u>US20050027179A1</u>	Biosensor and methods of use thereof	Cygnus, Inc.
<u>US6850790</u>	Monitoring of physiological analytes	Cygnus, Inc.
<u>US20050049473A1</u>	Methods for estimating analyte-related signals, microprocessors comprising programming to control performance of the methods, and analyte monitoring devices employing the methods	Cygnus, Inc.
<u>US6862466</u>	Methods of monitoring glucose levels in a subject and uses thereof	Cygnus, Inc.
<u>WO05018443A1</u>	MICROPROCESSORS, DEVICES, AND METHODS FOR USE IN MONITORING OF PHYSIOLOGICAL ANALYTES	CYGNUS, INC.
<u>WO05011489A1</u>	PROCESSING ANALYTE SENSOR DATA	DEXCOM, INC.
Publication	Title	Assignee
<u>US20050043598A1</u>	Systems and methods for replacing signal artifacts in a glucose sensor data stream	DexCom, Inc.
<u>WO05012873A2</u>	ELECTRODE SYSTEMS FOR ELECTROCHEMICAL SENSORS	DEXCOM, INC.

<u>WO05012871A2</u>	INCREASING BIAS FOR OXYGEN PRODUCTION IN AN ELECTRODE SYSTEM	DEXCOM, INC.
<u>WO05011520A2</u>	OXYGEN ENHANCING MEMBRANE SYSTEMS FOR IMPLANTABLE DEVICES	DEXCOM, INC.
<u>US20050031689A1</u>	Biointerface membranes incorporating bioactive agents	DexCom, Inc.
<u>WO05010518A1</u>	ROLLED ELECTRODE ARRAY AND ITS METHOD FOR MANUFACTURE	DEXCOM, INC.
<u>US6862465</u>	Device and method for determining analyte levels	DexCom, Inc.
<u>WO05025634A2</u>	BIOINTERFACE MEMBRANES INCORPORATING BIOACTIVE AGENTS	DEXCOM, INC.
<u>WO05019795A2</u>	ELECTROCHEMICAL SENSORS INCLUDING ELECTRODE SYSTEMS WITH INCREASED OXYGEN GENERATION	DEXCOM, INC.
<u>US20050033127A1</u>	Wireless blood glucose monitoring system	Euro-Celtique, S.A.
<u>EP1502957A1</u>	Castable diffusion membrane for enzyme-based sensor application	F. Hoffmann-La Roche AG
<u>EP1502614A2</u>	Portable blood glucose meter and insulin infusion device	Health Hero Network, Inc.
<u>US6873865</u>	Method and apparatus for non-invasive blood constituent monitoring	Hema Metrics, Inc.
<u>US20050045476A1</u>	Systems and methods for blood glucose sensing	Home Diagnostics, Inc.
<u>US6862091</u>	Illumination device and method for spectroscopic analysis	InLight Solutions, Inc.
<u>US6858401</u>	Minimum procedure system for the determination of analytes	LifeScan, Inc.
<u>US6856125</u>	Biosensor apparatus and method with sample type and volume detection	LifeScan, Inc.
<u>US6855243</u>	Electrochemical test strip having a plurality of reaction chambers and methods for using the same	LifeScan, Inc.
<u>EP1510555A1</u>	8-(anilino)-1-naphthalenesulfonate analogs and their use in analyte detection assays	Lifescan, Inc.
<u>US6872299</u>	Passive sample detection to initiate timing of an assay	LifeScan, Inc.
<u>US6872298</u>	Determination of sample volume adequacy in biosensor devices	LifeScan, Inc.
<u>US6863801</u>	Electrochemical cell	LifeScan, Inc.
<u>EP1510171A1</u>	Analytical device with prediction module and related methods	LifeScan, Inc.
<u>US6860978</u>	Biosensor and method of producing the same	Matsushita Electric Industrial Co., Ltd.
Publication	Title	Assignee
<u>EP0965301B1</u>	Electrode probe and body fluid examination equipment including the same	Matsushita Electric Industrial Co., Ltd.
<u>US20050027177A1</u>	Real time self-adjusting calibration algorithm	Medtronic Minimed, Inc.
<u>US6873268</u>	Microprocessor controlled ambulatory medical apparatus with hand held communication device	Medtronic Minimed, Inc.
<u>US20050065556A1</u>	Implantable multi-parameter sensing system and method	Medtronic MiniMed, Inc.
<u>US20050065465A1</u>	Safety limits for closed-loop infusion pump control	Medtronic MiniMed, Inc.
<u>US20050065464A1</u>	System for providing blood glucose measurements to an infusion device	Medtronic Minimed, Inc.
<u>WO05011490A1</u>	IMPLANTABLE BIOSENSOR	Medtronic, Inc.

<u>US20050049472A1</u>	Implantable biosensor devices for monitoring cardiac marker molecules	Medtronic, Inc.
<u>WO05020797A2</u>	IMPLANTABLE BIOSENSOR DEVICES FOR MONITORING CARDIAC MARKER MOLECULES	Medtronic, Inc.
<u>US20050056539A1</u>	Implantable sensor electrodes and electronic circuitry	Medtronic-Minimed, Inc.
<u>WO05015184A1</u>	REFLECTION HOLOGRAM SENSOR IN CONTACT LENS	Novartis AG
<u>US6850786</u>	Ocular analyte sensor	Novartis AG
<u>US6862534</u>	Method of determining an analyte concentration in a sample from an absorption spectrum	OptiScan Biomedical Corporation
<u>WO05016125A2</u>	METHOD AND APPARATUS FOR BODY FLUID SAMPLING WITH INTEGRATED ANALYTE DETECTING MEMBER	PELIKAN TECHNOLOGIES, INC.
<u>US6849237</u>	Body fluid test apparatus with detachably mounted portable tester	Polymer Technology Systems, Inc.
<u>US6853854</u>	Noninvasive measurement system	Q Step Technologies, LLC
<u>US20050059871A1</u>	Tissue implantable sensors for measurement of blood solutes	Regents of the University of California
<u>WO05012900A1</u>	BIOSENSOR WITH MULTIPLE ELECTRICAL FUNCTIONALITIES	ROCHE DIAGNOSTICS GMBH
<u>US6852500</u>	Method for determining the concentration of glucose in a body fluid with glucose-containing perfusate	Roche Diagnostics GmbH
<u>WO05026178A2</u>	ELECTROCHEMICAL AFFINITY BIOSENSOR SYSTEM AND METHODS	ROCHE DIAGNOSTICS GMBH
<u>WO05017571A2</u>	OPTICAL IN VIVO ANALYTE PROBE USING EMBEDDED INTRADERMAL PARTICLES	SKYMOON RESEARCH & DEVELOPMENT
<u>WO05012553A2</u>	OPTICAL IN VIVO PROBE OF ANALYTE CONCENTRATION WITHIN THE STERILE MATRIX UNDER THE HUMAN NAIL	SKYMOON RESEARCH & DEVELOPMENT
<u>US20050027176A1</u>	Optical in vivo analyte probe using embedded intradermal particles	Skymoon Research & Development, LLC
<u>US20050043597A1</u>	Optical vivo probe of analyte concentration within the sterile matrix under the human nail	Skymoon Research and Development, LLC
Publication	Title	Assignee
<u>US20050037483A1</u>	Vacuum device for substance extraction	SpectRx, Inc.
<u>WO05017495A2</u>	INTERFEROMETRIC SENSOR FOR CHARACTERIZING MATERIALS	UNIVERSITY OF CENTRAL FLORIDA
<u>WO05024416A1</u>	WATER SOLUBLE BORONIC ACID FLUORESCENT REPORTER COMPOUNDS AND METHODS OF USE THEREOF	WANG, Binghe
<u>US20050042135A1</u>	Devices for analyte concentration determination and methods of manufacturing and using the same	
<u>US20050038674A1</u>	System and method for managing a chronic medical condition	
<u>US20050038329A1</u>	Methods and kits for assays of rapid screening of diabetes	
<u>US20050033148A1</u>	Module for a computer interface	

US20050026302A1 Combining transmittance detection and chromatographic strip techniques providing a simple, easy, sensitive, accurate, fast and inexpensive way to quantitate analytes in biological fluid

US20050023154A1 Determination of sample volume adequacy in biosensor devices

US20050023152A1 Devices and methods relating to electrochemical biosensors

US20050023137A1 Biosensor with multiple electrical functionalities

US20050023136A1 Reduced volume electrochemical sensor

US20050043630A1 Thermal Emission Non-Invasive Analyte Monitor

US20050043603A1 Non-invasive blood glucose monitoring system

US20050037482A1 Dual measurement analyte detection system

US20050037384A1 Analyte detection system

US20050036147A1 Method of determining analyte concentration in a sample using infrared transmission data

US20050036146A1 Sample element qualification

US20050030540A1 Optical spectroscopy apparatus and method for measurement of analyte concentrations or other such species in a specimen employing a semiconductor laser-pumped, small-cavity fiber laser

US20050027183A1 Method for non-invasive monitoring of blood and tissue glucose

US20050023484A1 Device for the simultaneous detection of radiation of different wavelengths

US20050027463A1 System and methods for processing analyte sensor data

US20050027462A1 System and methods for processing analyte sensor data

US20050043275A1 Detection of glucose in solutions also containing an alpha-hydroxy acid or a beta-diketone

US20050042704A1 Entrapped binding protein as biosensors

US20050038332A1 System for monitoring physiological characteristics

US20050033132A1 Analyte measuring device

US20050027182A1 System for monitoring physiological characteristics

US20050027181A1 System and methods for processing analyte sensor data

US20050027180A1 System and methods for processing analyte sensor data

US20050027175A1 Implantable biosensor

US20050065760A1 Method for advising patients concerning doses of insulin

US20050054082A1 Analysis system for determining an analyte concentration, taking into consideration sample-and analyte-independent light-intensity changes

US20050065416A1 Non-invasive measurement of blood glucose level

US20050064528A1 Non-or minimally invasive monitoring methods

US6868285 Method and device for detecting substances in body fluids by Raman spectroscopy

US20050054908A1 Photostimulation method and apparatus in combination with glucose determination

<u>US20050054907A1</u>	Highly portable and wearable blood analyte measurement system
<u>US20050054906A1</u>	Spatial detectors for in-vivo measurement of bio chemistry
<u>US20050049466A1</u>	Optical sampling interface system for in vivo measurement of tissue
<u>US20050064529A1</u>	Diagnostic sensing apparatus
<u>US20050056552A1</u>	Increasing bias for oxygen production in an electrode system
<u>US20050054909A1</u>	Oxygen enhancing membrane systems for implantable devices
<u>US20050051440A1</u>	Electrochemical sensors including electrode systems with increased oxygen generation

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