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Closed Loop Automated Insulin Delivery Systems: From DIY to FDA Approved

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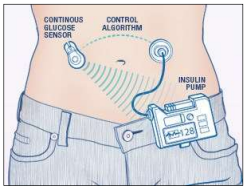
Automated Insulin Delivery

AID (aka Artificial Pancreas) devices use CGM data inputs to drive automated changes to insulin delivery through an insulin pump



Automated Insulin Delivery

- Many still struggle to maintain good glycemic control
- Hypoglycemic unaware individuals at risk
- Risk of nighttime hypoglycemia
- Better quality of life needed

FDA believes that development of AID devices will improve outcomes for people with diabetes

Automated Insulin Delivery

Challenges:

- Device limitations – pump imprecision, sensor inaccuracy/unreliability
- Biology – complicated
- Inter-individual variability – one size doesn't fit all. Smart algorithms?

Good news - Brilliant people working on these challenges….

How we got here…

- Where we were 15 years ago
- CGM approval/improvement
- Open loop studies / Algorithm development
- Compensating for CGM/pump failures
- Gradually increasing confidence in algorithms

Today

- AID devices are transitioning from feasibility to the pivotal/commercial space
- Previous focus on algorithm development/tweaking

- Attention now on how to translate discoveries into real devices
- Investigators thinking more about commercialization

Very significant times!

Types of AID Systems

- Insulin only
- Bi-hormonal (e.g., insulin and glucagon)

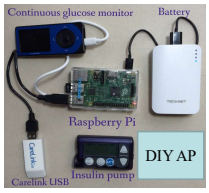
- Hypo/hyper minimizers
- "treat-to-target"
- "Hybrid" closed loop (still need meal bolus)
- Fully closed-loop AID systems (no/little intervention)

"DIY" AID Devices

•Patients are building their own AID systems and sharing that information online

•"Distribution" has many forms

•FDA Enforcement by Public Risk



Red Flag or Red Tape?

Red Flags or Red Tape?

Responsible Party - Who is responsible? AP developer? CGM developer? Pump developer? No one?

Design Control - Modified AP software code that is incompatible with rarely used pump setting causes bolus calculator to use incorrect value for Insulin On Board

Human Factors - AP app designed so that users may inadvertently hit bolus button when intending to input meal data

Safety Mitigations - Software that incorrectly calculates small insulin doses required for children not discovered until serious adverse event occurs (outside of a clinical trial with monitors)

Postmarket - AP Users reports problem on #APtwitterhandle, but due to high volume of tweets, it is not seen/tracked/dealt with

"DIY" AID Devices

•Patients' cry for help – Give us technology that should be available to me!

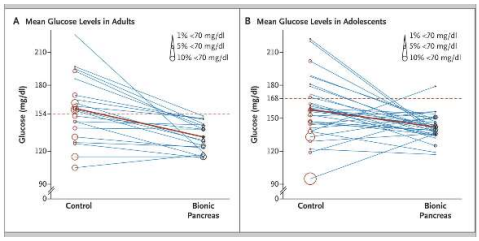
•We recognize the need for:

- •Smooth and efficient pathways for technology
- •Efficient clinical trials

Let's create a situation so patients don't feel compelled to do this…

"Bionic Pancreas"

(Beta Bionics)



Russell, et al., Outpatient Glycemic Control with a Bionic Pancreas in Type 1 Diabetes, N Engl J Med, 2014

"Bionic Pancreas"

(Beta Bionics)

Home use study (AID vs. insulin pump):

- reduction in mean glucose level (162 ± 29 vs 141 ± 10 mg/dL, *P*<.0001)
- reduced percent time <60 mg/dL (1.9 ± 1.7 vs 0.6 ±0.6%,*P*<.0001)
- reduction in the mean number of symptomatic hypoglycemia events per day (0.59 ± 0.56 vs 0.90 ± 0.64 events per day, *P*=.023)

Presented at ADA Annual Meeting 2016

670G Hybrid Closed Loop System
(Medtronic)

Adolescents and Adults had spent 3 months on the system

Medtronic reported, compared to "open loop" performance:

- 0.5% reduction in A1c (from 7.4% at start to 6.9% at end)
- 44% reduction in time spent < 70 mg/dl
- 40% reduction in time spent < 50 mg/dl
- 11% reduction in time spent >180 mg/dl
- 8% increase in time spent between 71-180 mg/dl

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Presented by Medtronic at ADA Annual Meeting 2016

What does FDA Consider?

Artificial Pancreas devices do not have to be perfect with zero risk to be beneficial

- Approval decision is a benefit/risk decision
- Approval Decision made in the context of the significant risks people with diabetes face every day due to their disease

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Challenges

- Promotion of innovative AID devices requires smooth device development processes and efficient regulatory pathways

- "Business as usual" for both FDA and device manufacturers will not allow innovations to get to patients in a timely manner
- Creative and cooperative solutions are needed

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The Vision:
Improve Interoperability and Make it Feasible

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- Traditional pathway = one company sells whole AID device (sensor, pump, algorithm)
- Alternate pathway = different companies sell the components of an AID device (e.g., algorithm on app that communicates with pump and sensor)
- More choices/access
- Working on Policies to Foster this Innovation:
  - Who is responsible? (for adverse events, etc.)
  - Impact of Device modifications/generations

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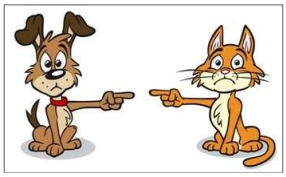
Regulatory Challenges



Device Failure: Who is responsible?

Algorithm developer? CGM developer?

Pump developer? No one?

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Regulatory Challenges

Responsible Party:

- Need to assure all bases are covered
- No patients "falling through the cracks"
- Responsible party can receive feedback/complaints, and provide relief

Regulatory expectations need to be defined – Who is responsible for what when multiple components form a system?

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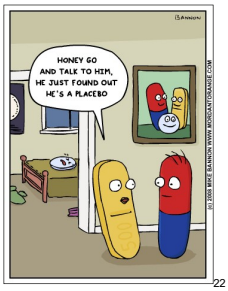
Regulatory Challenges

- Some AID devices will require novel drugs or drug formulations
- Sponsors need to talk to FDA early to understand testing requirements for drug approval



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Regulatory Challenges

Modifications:

- Devices must continue to be compatible and fulfil necessary specifications when one is modified
- Standards can help identify methods and criteria to validate modifications
- Regulatory "definitions" may also help (e.g., "AID-ready" CGM or pump)

How can devices be modified and remain safe in a system when developers are not working together?

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Access Challenges

Insurance Coverage

- We encourage developers to think of this early
- Studies to support coverage are typically sufficient for FDA as well
- Most companies put this off until after FDA approval

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Device Communication

Standardized communication will enable parallel FDA submissions

- What type of data should be used? (Sensor values? Glucose concentrations? Both?)
- Communication protocols? Authentication?
  Handshakes?
- Cybersecurity standards?
- Validation standards and acceptance criteria?

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Training Challenges

- Clinicians will need training as well as patients
- How can I train my patients if I don't understand what the device can and can't do?

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Training Challenges

- Newly diagnosed who start on an AID system – will they understand how to use insulin (e.g., when the device fails)?

Not yet enough discussion about how the diabetes community will integrate AID devices

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How do you handle patients who come to you with DIY AID devices?

These devices have not been determined to be safe and effective

Good questions to ask:

- Do you understand EXACTLY what algorithm is being used? Is it right for you?
- Have you checked the code to ensure it implements the algorithm correctly? Have you double checked?
- When new, modified versions of code are shared, have you re-validated your entire system before implementing it?
- Etc…

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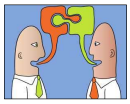
What Can You Do To Help Promote AID Systems?

- Provide input on pain points, goals, requirements for new AID systems
- Help identify patient and HCP needs



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Where do we go next?

- Continue to work with Investigators and Companies who are developing these devices to encourage their development
- Continue to learn from patients and healthcare providers about the needs and desires of this community
- Continue to develop policies that promote rather than prohibit AP availability

We are close to the first finish line…

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Our first commercial AID system is about to be born…

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The real work begins…now we have to learn how to raise it!

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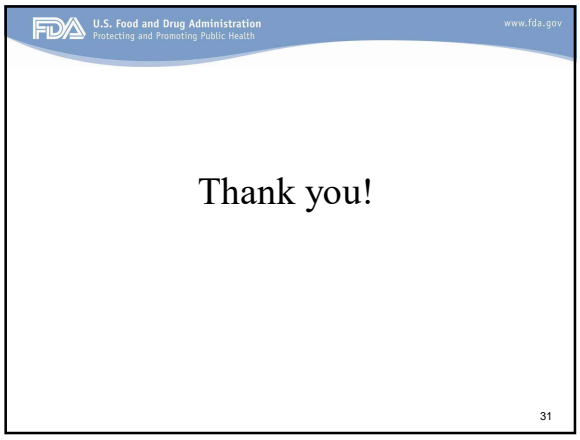
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Thank you!
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