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MEETING PROCEEDINGS

Insulin Pump Safety Meeting: Summary Report

David C. Klonoff, M.D., FACP[1] and Juliet S. Reyes, B.S.[2]

Abstract

Diabetes Technology Society convened a panel of insulin pump experts in Bethesda, Maryland, on November 12, 2008, at the request of the Food and Drug Administration. The group consisted of physicians, nurses, diabetes educators, and engineers from across the United States. The panel members (1) discussed safety features of insulin pump therapy and (2) recommended adjustments to current insulin pump design and use to enhance overall safety. Software and hardware features of insulin pumps were analyzed from engineering, medical, nursing, and pump-user perspectives. The meeting was divided into four sections: (1) Engineering Safety—Designing Software and Hardware for Insulin Pump Therapy; (2) Patient Safety—Selecting Patients and Clinical Settings for Insulin Pump Use; (3) Clinical Safety—Determining and Delivering Insulin Dosages Using Insulin Pump Therapy; and (4) Personal Experiences—A Panel Discussion about Insulin Pump Safety. Six aspects of insulin pump technology were noted to present potential safety problems: (1) software, (2) wireless communication, (3) hardware, (4) alarms, (5) human factors, and (6) bolus-dose calculation. There was consensus among meeting participants that insulin pump therapy is beneficial in patients of all ages and that insulin pump safety must be assured through careful regulation.

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Introduction

This meeting was conducted to assess the safety of insulin pumps and to make recommendations for improving insulin pump design to ensure the safety of each patient who uses insulin pump therapy. David C. Klonoff, M.D., FACP, from Mills-Peninsula Health Services in San Mateo, California, provided welcoming remarks and stated that it will be important for the Food and Drug Administration (FDA) to begin looking at insulin pumps in a systematic way, after having made decisions on individual products for many years. Commercially available insulin pumps have become increasingly complicated. They contain many new features that might not interact seamlessly in every situation. This may be a good time to revisit insulin pump performance and to analyze various features of insulin pumps systematically for their safety. Larry Kessler, Sc.D., from the FDA in Silver Spring, MD, provided introductory remarks. He reviewed the various components of insulin pumps that must be regulated by the FDA. He then discussed the increasingly important problem of electromagnetic interference, which can potentially degrade the performance of any effector medical device, such as an insulin pump, especially if the device is controlled wirelessly.

Author Affiliation: [1]Mills-Peninsula Health Services, San Mateo, California; and [2]Diabetes Technology Society, Foster City, California

Abbreviations: (BG) blood glucose, (CGM) continuous glucose monitor, (FDA) Food and Drug Administration

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Corresponding Author: David C. Klonoff, M.D., FACP, Mills Peninsula Health Services, 100 South San Mateo Drive, San Mateo, CA 94401; email address *dklonoff@yahoo.com*

Session 1: Engineering Safety—Designing Software and Hardware for Insulin Pump Therapy

Paul Jones, M.S.C.E., C.D.P., CSQE, from the FDA in Silver Spring, MD, was the moderator of this session.

Judith U. Cope, M.D., M.P.H., from the FDA in Rockville, MD, spoke about a recently published postmarket analysis of adverse events that have been reported with insulin pump use.[1] From 1996 through 2005, the FDA received 1594 reports of adverse events involving insulin pumps in patients between the ages of 12 and 21 years. These adverse events involved injuries in 1038 patients (65.1%), malfunctions in 528 patients (33.1%), "other events" in 15 patients (0.9%), and death in 13 patients (0.8%). The device-related events involved error messages as well as problems with the alarm, catheter, and/or screen display. Among 102 events due to patient-related causes, most were related to inadequate education (47) and nonadherence/noncompliance (19). Other factors involved in adverse events included various sports (12), device misuse (8), inadequate responsibility and care for the device (5), and risk-taking behaviors (4). No information was collected on the total number of pump users during this period, thus the incidence of such complications could not be calculated.

Dorian Liepmann, Ph.D., from the University of California at Berkeley in Berkeley, CA, discussed engineering and environmental considerations for insulin pump hardware. He pointed out that the two main factors hindering development of closed-loop control are the delay in absorption of insulin from the subcutaneous tissue and the time delay of a glucose response to insulin. He felt that the primary engineering problem to be solved is how to measure the flow rate of insulin to trigger an alert in case of a tubing blockage or an unprogrammed change in this flow rate. He suggested an inline sensor that could measure insulin flow. To compensate for mechanical problems, he suggested the use of: (1) wireless technology to communicate with a cell phone that could automatically call for assistance; (2) data storage to detect out-of-range blood glucose (BG) values; and (3) a valve system to turn off the device automatically in the event of a pump malfunction.

Paul Jones presented an overview of the FDA's infusion safety software and system safety research program. He pointed out that safety standards for insulin pumps are of increasing interest at his agency. Mr. Jones also stated that the FDA is planning to design a generic infusion pump software model that should capture all the safety considerations. Manufacturers and designers will be allowed to add or subtract to it in order to arrive at a reasonable safety standard.

This session was concluded with a presentation by Raoul Jetley, Ph.D., from the FDA in Silver Spring, MD, on a formal-methods-based model for the generic infusion pump. The purpose of creating a generic insulin pump model is to develop a reference model for insulin pump software. This plan will allow manufacturers to add and run their own permutations on the generic pump model that will be composed of separate components. With this model system in place, engineers will be able to substitute their own components to the model and test their devices for software errors without a patient.

Session 2: Patient Safety—Selecting Patients and Clinical Settings for Insulin Pump Use

Wayman Wendell Cheatham, M.D., FACE, from the Bureau of Medicine and Surgery, U.S. Navy, in Washington DC, was the moderator of this session.

William Tamborlane, M.D., from Yale University in New Haven, CT, spoke about the benefits associated with insulin pump use in children and adolescents. He presented evidence that insulin pump therapy improves control, decreases complications, and enhances the quality of life of the parents of pediatric diabetes patients.

Robert Bernstein, M.D., FACE, from Regional Endocrinology Associates in Santa Fe, NM, spoke about the benefits of insulin pump therapy in adults. He noted that the problems encountered during insulin pump therapy are caused by patient error in over 95% of cases. He stated that the most common safety problems in adults are: (1) pump damage from cracking or damaging the holster followed by either immersion in water or exposure to heat in a sauna or hot tub, all leading to pump damage; (2) failing to connect the tubing securely to an infusion set after having disconnected the unit for a shower or physical intimacy, in which case the pump continues to infuse insulin, but the patient might not notice an insulin leak; (3) leaking caused by the catheter dislodging from the skin, with similar consequences as the previous problem; (4) using an infusion set for more than three days; (5) failing to rotate infusion sites; (6) disregarding alarms; (7) failing to test BG levels and/or using inappropriate bolus doses; (8) overriding the bolus calculator software to avoid overdosing, which usually

results in underdosing; (9) guessing rather than counting carbohydrates; and (10) forgetting to activate a bolus dose. He emphasized patient selection and patient education to avoid insulin pump problems.

Curtiss Cook, M.D., from the Mayo Clinic College of Medicine in Scottsdale, AZ, spoke about insulin pump therapy in the hospital. He pointed out that hospital staff members must be provided with guidelines that will allow their patients to continue with their insulin pump therapy in the hospital and ensure safety while they are inpatients. He described the procedures that have been implemented at the Mayo Clinic in Scottsdale to facilitate safe pump usage for patients receiving treatment in their facility (see **Table 1**). Dr. Cook stated that there have been no adverse events reported in the Mayo Clinic in Scottsdale with patients continuing insulin pump therapy during hospitalizations. Furthermore the frequency of hypoglycemic events was lower in patients who continued pump therapy than in those who did not continue with pump therapy while hospitalized. He concluded that guidelines should also be provided for insulin pump use in hospitalized children and in delicate situations, such as during surgery or labor.

Table 1.
Current Procedures for Patients Admitted on Insulin Pump Therapy[a]

Medical staff indentifies presence of insulin pump, brand of pump, and insulin type
Blood or capillary glucose level is determined
Contraindications for continued insulin pump are assessed
Physician order for alternative insulin therapy is obtained if CSII must be discontinued
Admitting physician writes initial order for insulin pump therapy using the preprinted order form
Endocrinology, diabetes educator, and nutrition consults ordered by admitting physician
Insulin Pump Basal/Bolus Blood Glucose Record flow sheet is placed at bedside.

[a]Reprinted from Leonhardi and colleagues[2] with permission.

Session 3: Clinical Safety—Determining and Delivering Insulin Dosages Using Insulin Pump Therapy

Tonja Nansel, B.S.N., Ph.D., from the National Institutes of Health, Eunice Kennedy Shriver National Institute of Child Health and Human Development in Bethesda, MD, was the moderator of this session.

Susanne Brown, R.N., B.S.N., CDE, from the Diabetes and Endocrine Center, Upper Chesapeake Health in Bel Air, MD, spoke about insulin dosing algorithms, insulin on board, and bolus calculators. She discussed the benefits of industry-wide standards for embedded algorithms that calculate insulin boluses for hyperglycemia, and she noted that different pumps contain different types of bolus-dosing software. In addition, devices can be programmed individually to administer insulin using different rules. For example, the 1500 rule and the 1900 rule can both be used to calculate a total daily insulin dose, and the two doses will be different. Because recommended bolus dosages have varied among manufacturers, Ms. Brown recommended that companies be required to publish their dosing formulas. Although a bolus calculator in an insulin pump is useful for determining a bolus dose, there are no standards to consistently account for insulin on board or the duration of action of a previous insulin bolus. Although some pumps can deliver a variety of basal rates, there is no mechanism that requires patients to reset their basal rate and total daily dose to the lowest levels after situations when higher doses are needed. She expressed concern regarding a feature that allows a hasty bolus without a patient having to look at the screen or use the bolus calculator. These remote-controlled or button-controlled boluses may not be suitable for some patients.

Many questions remain unanswered. What basal level and bolus dosage will work best for a patient who is extremely resistant to insulin? What is the best way to compute the insulin-to-carbohydrate ratio? How does one account for hormonal changes, menstrual cycles, exercise, and stress? What exact procedures should be followed with unexpectedly high glucose values? The absence of standards in these aspects of insulin pump therapy has led to errors in the programming of devices. It may be prudent to eliminate the manual mode on these devices. Ideally health care providers would be able to lock in certain features of the pump within a range that is determined individually for each patient. Patient education on insulin pump use must also be standardized (e.g., regarding pharmacokinetic and pharmacodynamic factors of insulin as well as peak levels and duration of action of insulin). Health care providers must be consistent in their education on the safe use of insulin pumps and should accrue ample evidence that a patient is diligent before they recommend pump therapy. Also, manufacturers can supplement basic education programs by using the device itself to explain the importance of each device feature until the patient overrides the message with a prompt stating, "Do not show this message again."

Diane Hatcher, M.S., R.N., CPNP, CDE, from the Walter Reed Army Medical Center in Washington DC, spoke about alarms, hypoglycemia prevention, and troubleshooting. The problem of communicating vital information to the patient via alarms can be viewed from many angles. From an engineering standpoint, the device can be packed with many "bells and whistles" to make it more appealing and convenient for users. However, from a clinician's perspective, it does not matter what types of alerts are delivered, because the patient might be unable or unwilling to react appropriately. For any pediatric patient or an adult who may be sleeping during the alarm, either voice alarms or differentiating alarms (e.g., a louder alarm or a stronger vibration) can be added to alert parents or other household members to the problem. Also, if a user disconnects from the device for any reason, then the alarm should sound loudly enough to remind the user of the disconnection and any missed boluses. Finally, because of electromagnetic interference and physical obstacles, alarms would be more helpful if they were transmitted via multiple frequencies.

Christine Kessler, R.N., M.N., CNS, ANP, BC-ADM, from the Walter Reed Army Medical Center, DeWitt Army Community Hospital in Washington DC, spoke about remote-control devices, interfaces with glucose monitors, and interfaces with personal computers. Wired and wireless environments, radio frequency waves, electromagnetic interference, external radiation, and infrared communications are examples of technology that can invisibly affect the performance of a patient's device. It is very common now to see many sensors and readers installed in various locations to monitor movement of people and/or objects. This technology is being used in nursing homes where patients might already be wearing devices for controlling heart rhythm or drug delivery, such as implantable pacemakers and drug infusion pumps. Patients might be exposed to danger if common radiofrequency-emitting devices, such as cell phones, microwave ovens, metal detectors, or medical imaging equipment, should inadvertently interfere with the proper performance of a personal medical device. It is crucial that patients be protected from possible malfunction of their devices due to electromagnetic interference produced by other devices. Connectivity and interface problems can degrade performance of medical devices such as insulin pumps. The first manifestation of this type of problem can be in the collection of data. Most patients are not adept with using a computer for medical data uploading. Many patients prefer to use handwritten BG logs, but they often forget to record their information, or they might fabricate data. When patients do maintain their own database on a personal computer, then their health care providers usually do not have immediate access to the information. Sometimes patients themselves cannot access their information if their computer system is broken or if they are traveling. Although some Internet sites are intended for file sharing, many patients are hesitant to use them because of privacy and security concerns. For patients who are military personnel, security measures completely forbid the use of the Web to transmit medical data. Many patients are leery of telemedicine because of the threat of losing their privacy to hackers and eavesdroppers. Cell phones are becoming increasingly popular for transmitting medical data, because many patients feel less vulnerable transmitting their personal data when using these devices compared to computers.

For those who use glucose monitors and personal computers to collect data, there is still the problem of transmitting this information to the physician in a timely, accurate, readable format. Incompatibility of device ports and software is rampant. Some devices use USB ports, while others use only infrared. A patient may use a certain proprietary software system that bars a physician from reading the patient's data. Even when transmissions are successful, time discrepancies present another problem. Three reasons for discrepant or inaccurately recorded time data are: (1) a change of battery in a device; (2) travel to a different time zone; or (3) electromagnetic interference. As a result BG data may be shifted into a wrong time bucket. For example, data might appear as prebreakfast values when in fact the data sent were from evening measurements. If the times of the meter and the pump are programmed incorrectly, then the downloaded data are inaccurate and can lead to inappropriate treatment.[3]

Overall the insulin pump is a unique medical device because of the extent to which patients interact with it and intervene in its operation. If manufacturers will modify insulin pumps to easily interface with other devices, then patients will experience improvements in the collection, transmission, retrieval, and interpretation of data, and these improved interfaces will result in timely communication between health care providers and their patients.

Irina Nayberg, R.N., B.S.N., CDE, from Mills-Peninsula Health Services in San Mateo, CA, spoke about insulin pump safety during clinical trials. She explained how participants wearing insulin pumps during an insulin infusion, which is part of a glucose clamp study, will

frequently disconnect their pumps and let the insulin drip onto their clothing or a pad. These patients elect to disconnect rather than disable the pump and have to deal with a disconnect alarm. When it is time for bolus, they will have less basal insulin in their bodies than a bolus calculator program would have accounted for, because these calculators only account for bolus insulin on board and not for the presence or absence of basal insulin on board. The result is typically an inadequate bolus dose, and the result of this is an episode of hyperglycemia. Ms. Nayberg recommended that a safety feature be built into an insulin pump that notes a decrease or stoppage of flow and calculates the amount of missed basal insulin, which in turn is subtracted from the calculated amount of insulin on board.

Session 4: Personal Experiences—A Panel Discussion about Insulin Pump Safety

Christine Kessler, R.N., M.N., CNS, ANP, BC-ADM was the moderator of this session.

A discussion, by five patients with type 1 diabetes who attended the meeting, highlighted benefits and safety problems with insulin pumps. The duration of their insulin pump use ranged from 3 to 43 years. Human factor (i.e., ergonomic) problems were identified, including small screens, small fonts, dark screens, alarms with too little sound or too little vibration, and poorly placed buttons. All participants of the meeting were invited to submit a list of suggestions for improving any aspect of insulin pump safety. The 44 submitted suggestions were classified as being related to: (1) software; (2) hardware; (3) alarms; (4) device connection and flow detection; (5) education and training; and (6) manufacturers and regulators. The suggestions are listed as follows.

Device Features:

Software:

- Allow the patient to customize features such as alarms, visual display, and degree of complexity so that the device can be matched to the patient's capabilities, needs, and limitations.
- Provide variable volume settings and tones for alarms.
- Provide menus that are more intuitively obvious.
- Standardize data formats.
- Enable automatic time synchronization between pumps and other medical devices such as meters and continuous glucose monitors (CGMs).
- Solve the time discrepancy issues in the same way a cell phone does.
- Design insulin pumps or CGMs to allow data input regarding diet, exercise, and stress.
- Build a graphic bolus counter instead of just using beep sounds to confirm exactly how many doses a patient has received.
- Install an antistacking feature. This would be useful because users look at only the most recent bolus. This feature would allow the clinician to make decisions with the patient to prevent stacking and hypoglycemia.
- Use the cell phone camera to count carbohydrates.
- Improve accuracy of pumps to deliver programmed doses of insulin.
- Provide graphs of downloaded glucose levels from BG monitors and CGMs.
- Allocate an area for the patient and the physician to enter comments in the electronic logs that are available for download.
- Make software more available and reasonably priced for the public. Proprietary issues increase the cost of everything.
- Improve the accuracy of the pump's communication with the meter and CGM.

Hardware:

- Produce devices with stronger vibrations.
- Use color in displays and make displays larger and more legible.
- Limit use, through software, to 3 days.
- Test accuracy and safety when using the pump in the highest heat of a desert climate such as Arizona.

Alarms:

These should sound when:

- the device is disconnected.
- the device is not switched to "suspend."
- a meal time has passed and no bolus was recorded.
- "Activate" is not used for an intended bolus.
- the device needs to be reset.

Device Connection and Flow Detection:

- Create an alarm for when the pump is disconnected, and allow for backflow awareness.
- Create an alarm for insulin leakage or a blocked catheter.
- Develop an inline flow meter and pressure sensor to distinguish the lower pressure of extracorporeally redirected insulin flow from the higher pressure of appropriate subcutaneous insulin delivery.
- Allow the pump to be aware that a new infusion site is not functional (i.e., not absorbing insulin) and signal the user to change to another site.
- Improve the quality of cannulas so there is less likelihood of crimping.
- Mandate the AUTO OFF function. Currently it is optional.
- Following manual discontinuation, allow the user to manually input the total amount of time disconnected from the pump.
- When a pump is disconnected, the pump should have to be on "suspend" or else the pump must be able to detect that the basal delivery has been interrupted.
- Increase durability, especially for children, so the tubes do not pull out while the patient is sleeping or playing sports.

Education and Training:

- Require more education before allowing patients to use the pump.
- Provide more guidance for groups with special-needs patients.
- Implement better support systems for pump users, including continuing education.
- Instruct patients to report adverse events to the manufacturer or the FDA. This is a significant missing link in communication. Patients are the most neglected and important link in providing feedback and reporting adverse events that will help in future designs of insulin pumps.
- Both the government and the manufacturers should provide more information and statistics regarding different products already available or in development so physicians and patients can make more informed choices.

Manufacturers and Regulators:

- The FDA should be stricter regarding the marketing and use of these devices. Companies do not accurately promote their pumps. They also select the wrong candidates and do not train them adequately.
- The government should release an official report comparing all pumps, BG monitors, and CGMs.
- A database and national repository should be created to record and provide complete data on the numbers of patients with diabetes on multiple daily injections versus insulin pumps and the percentages in each group that experience or do not experience adverse events. The reporting and publication of only the numbers of adverse events associated with pumps provides an incomplete assessment. Perhaps the FDA can expand medical tracking or monitoring of patients.
- Systematically provide information to schools so they can better accommodate students with pumps. Rules vary from school to school and should address issues such as whether patients can test while in the classroom if they are hypo- or hyperglycemic or if the insulin level in the pump is low and whether they should be allowed to walk to the nurse's office. Teachers and coaches should also be made aware that alarms may sound like cell phones, as patients are often reprimanded because the faculty mistake alarms for phones.

- Consider a possible collaboration between device manufacturers with a company such as Apple, Inc. that could lead to the development of an "iPump," a device similar to the iPod, that integrates the latest technology and algorithms to provide user-friendly features to insulin pump users.

- Minimize the impact of human errors with closed-loop insulin delivery.

Conclusions

The panel concluded that insulin pumps are generally safe and effective for controlling diabetes. Potential safety problems exist in six elements of these devices. These aspects are: (1) software (2) wireless communication, (3) hardware, (4) alarms, (5) human factors, and (6) bolus-dose calculation. There was consensus among meeting participants that insulin pump therapy is beneficial in patients of all ages and that pump safety must be assured through careful regulation.

Panel Members:

Chair: **David C. Klonoff, M.D., FACP,** Mills Peninsula Health Services, San Mateo, California

Robert Bernstein, M.D., FACE, Regional Endocrinology Associates, PC, Santa Fe, New Mexico

Susanne Brown, R.N., B.S.N., CDE, Diabetes and Endocrine Center, Upper Chesapeake Health, Bel Air, Maryland

Wayman Wendell Cheatham, M.D., FACE, Bureau of Medicine and Surgery, U.S. Navy, Washington DC

Curtiss Cook, M.D., Mayo Clinic College of Medicine, Scottsdale, Arizona

Judith U. Cope, M.D., M.P.H., U.S. Food and Drug Administration, Office of Pediatric Therapeutics, Office of International Science Programs, Rockville, Maryland

Diane Hatcher, M.S., R.N., CPNP, CDE, Walter Reed Army Medical Center, Pediatric Endocrinology and Gastroenterology, Washington DC

Raoul Jetley, Ph.D., U.S. Food and Drug Administration, Center for Devices and Radiological Health, Office of Science and Engineering Laboratories, Silver Spring, Maryland

Paul L. Jones, M.S.C.E., C.D.P., CSQE, U.S. Food and Drug Administration, Center for Devices and Radiological Health, Office of Science and Engineering Laboratories, Silver Spring, Maryland

Christine Kessler, R.N., M.N., CNS, ANP, BC-ADM, Diabetes Institute, Department of Endocrinology and Metabolic Medicine, Walter Reed Army Medical Center, DeWitt Army Community Hospital, Washington DC

Larry Kessler, Sc.D., U.S. Food and Drug Administration, Director, Office of Science and Engineering Laboratories, Center for Devices and Radiological Health, Silver Spring, Maryland

Dorian Liepmann, Ph.D., Chair of the Bioengineering Department, University of California at Berkeley, Berkeley, California

Tonja Nansel, B.S.N., Ph.D., National Institutes of Health, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, Maryland

Irina Nayberg, R.N., B.S.N., CDE, Mills-Peninsula Health Services, San Mateo, California

William Tamborlane, M.D., Yale University, New Haven, Connecticut

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