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SYMPOSIUM

"No Coding" of Glucose Test Strips: A Roche Perspective

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Abstract

Introduction:

Glucose test strips vary slightly from batch to batch. These variations are accounted for by a batch-specific "code": a set of parameters defining the relationship between the signal change induced on the glucose test strip and the blood glucose concentration.

Methods:

We assessed the impact on accuracy of miscoding the ACCU-CHEK® Aviva system across a wide range of glucose test strip batches and glucose levels, throughout the shelf life of the glucose test strips.

Results:

The deviations in coding that we investigated had no effect on clinical action. Additionally, we showed, with mathematical modeling of a worst-case scenario, that the probability of an error altering clinical action is low. The batch-specific code of glucose test strips ensures the accuracy and safety of each blood glucose measurement. In addition to the parameters directly related to the blood glucose measurement, the electronic code chip contains the expiration date of the test strips and can deliver firmware updates for upgrades to the glucose meter.

Conclusions:

We eliminated the handling step of coding and retained all the advantages of coding. In Roche's newest all-in-one glucose meter, the ACCU-CHEK Compact Plus system, the batch-specific code is integrated into the drum that contains the glucose test strips. As a result, changing the drum containing the glucose test strips automatically changes the glucose test strip code. Patients with diabetes who use the ACCU-CHEK Compact Plus glucose meter do not have to be concerned with coding.

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Introduction

What happens when a patient with diabetes applies blood to a glucose test strip? First, in most glucose test strips today, the erythrocytes are separated from the rest of the blood.[1] Then, the fluid part of the blood containing the glucose to be measured passes into the reagent layer of the test strip. The reagent layer combines enzymes and other reagents to elicit a detectable signal change in the test strip. This signal change is evaluated by the glucose meter; and the blood glucose concentration is calculated and presented to the patient.

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This seemingly simple reaction in the test strip is a highly complex process and depends on several factors, including the absorption of the liquid by the reagent layer, the activity of the enzymes, and the sensitivity of the signal-detection method. The numerous raw materials used in the manufacturing process of glucose test strips and the influences to which they are subject can never be held constant—even when the manufacturing conditions are identical—that the same glucose concentration will always elicit the same signal change for every batch. Within each batch, however, the strip properties remain nearly constant. In glucose test strip manufacturing, therefore, the quality assurance department conducts an extensive series of measurements over the entire measurement range of the strip for every batch.

Methods

Basically, there are two methods for addressing batch-specific differences in the production process of glucose test strips. In the first method, the production differences are kept so small that their influence on the blood glucose measurement values is not clinically relevant. This means the manufacturer of the glucose test strips must adopt strict production tolerances and consequently reject batches of glucose test strips that do not conform to these stringent criteria.

The second method consists of using the measurements of the quality assurance department to establish a set of parameters that best defines the relationship between the signal change induced on the glucose test strip and the blood glucose concentration. This set of parameters defines the glucose test strip "code". In clinical evaluation of a glucose test system, the parameters that are encoded will already have been established and validated. Historically, coding processes have evolved from printed, changeable color scales that were adaptable to batch-specific conditions, batch-specific code numbers that have to be entered manually into the glucose meter, bar codes that are read by the glucose meter (**Figure 1**), to electronic code chips containing the batch-specific code (**Figure 2**).

Effects of Miscoding

Miscoding means that the glucose test strip code used does not contain parameters optimized to the particular batch of glucose test strips. This can result when patients either do not change the glucose test strip code or do not correctly match the test strip code to the test strips. We assessed the impact on accuracy of miscoding the ACCU-CHEK® Aviva glucose meter across a wide range of glucose test strip batches and glucose levels, throughout the shelf life of the test strips; we also evaluated the probability of severe errors that might affect clinical results.

Figure 1. The bar code on a drum of glucose test strips for Roche's ACCU-CHEK Compact Plus glucose meter. The bar code contains batch-specific code information.

Figure 2. An electronic code chip for Roche's ACCU-CHEK® Aviva glucose meter. The chip contains batch-specific code information.

Results

We analyzed 447 glucose test strip batches manufactured from February 2006 to July 2007, using a consensus error grid according to Parkes *et al.*,[2] with the following risk categories:

A. No effect on clinical action

B. Altered clinical action with little or no effect on clinical outcome

C. Altered clinical action—likely to affect clinical outcome

D. Altered clinical action—could have significant medical risk

E. Altered clinical action—could have dangerous consequences

The greatest concern focuses on errors that fall within risk categories C, D, and E, which all require altered clinical action and are considered extreme events. Errors that fall within risk categories A and B have little or no impact on clinical outcome. The worst-case prediction bias in a mismatch of the glucose test strip code and test strip was estimated for 6 representative glucose levels: 30 mg/dl, 50 mg/dl, 70 mg/dl, 180 mg/dl, 240 mg/dl, and 500 mg/dl. These estimates were calculated by mathematically modeling the influences of the wrong glucose test strip code parameters, the shelf life of test strips, and within-batch variability. These values were then plotted along the consensus error grid (**Figure 3**).

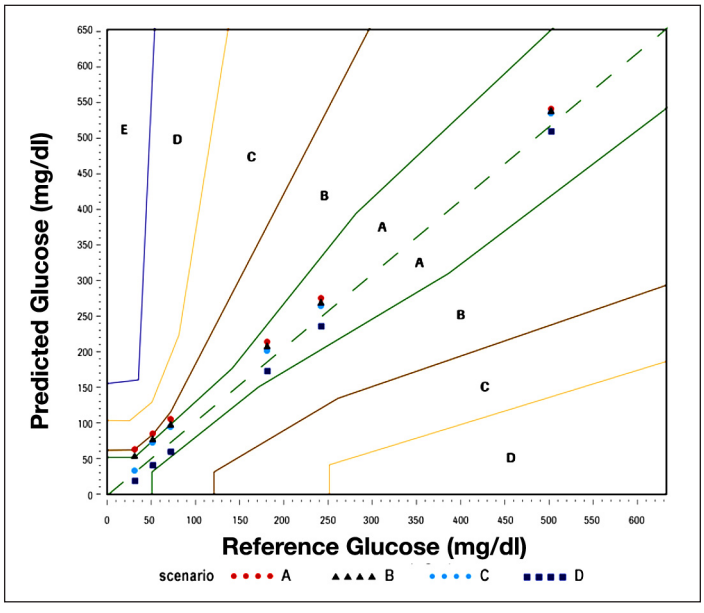

Figure 3. Estimated average bias of glucose test strip batches due to a mismatch of the test strip code and the test strip, using four extreme mismatch scenarios at six representative glucose levels.

Factors governing the estimated error rates included the probability of:

- A forced mismatch between the test strip code parameters and the test strip, which represents the largest divergence of performance based upon information from 447 glucose test strip batches
- A customer continuing to use an expired batch of glucose test strips
- The prevalence of blood glucose values <70 mg/dl

The overall probability of a risk category C event is the aggregate of the probabilities of each of these factors coming true. This was computed as the product of the individual probabilities. The only risk category C event that was likely to affect clinical outcome was a low glucose level (i.e., ≤70 mg/dl). The worst-case estimated likelihood of observing a category C error throughout the shelf life was calculated as 16.0 ppm. No values (actual or estimated) fell into risk categories D or E.

In addition to the theoretical modeling described earlier, a study was performed using spiked venous blood with four glucose solutions and two control solutions to assess the performance of extreme mismatches between the test strip code parameter and the test strip. Bias within this study ranged from ±15 mg/dl at glucose levels below 70 mg/dl to ±15% at higher glucose levels; these values fell within area A of the consensus error grid and support the results of the worst-case scenario simulated by the mathematical modeling. Maximum system accuracy requires correct glucose meter coding, reinforcing the need to code in accordance with the labeling instructions. However, this assessment with currently released lots demonstrates that even if the ACCU-CHEK Aviva glucose meter were miscoded, the probability of incorrectly altering a clinical action is low. (Roche Diagnostics. Effect of miscoding on ACCU-CHEK® Aviva system accuracy. Internal data 2007.) A study by Haak *et al.*, sponsored by Bayer, showed that the mean absolute deviation of the ACCU-CHEK Aviva glucose meter is 9.5%, if coded according to instructions, and 10.8% if miscoded. (Haak T, Gerlach H, Krichbaum M, Hermanns N. The effect of incorrect coding of blood glucose meters on the accuracy of blood-glucose self-testing Poster presentation. 2007.)

Advantages of Coding

What are the benefits for the diabetes patient of coding glucose test strips? The electronic code chip containing the batch-specific code can transmit additional information between the glucose meter and test strips (**Figure 4**).

This communication allows for easy upgrades to the glucose meter by providing firmware updates on the code chip. The following are examples of major upgrades to Roche's glucose meters conveyed via the code chip:

- The minimal blood volume required for a valid measurement of blood glucose is reduced.
- The reaction chemistry of the glucose test strips is altered.
- The blood glucose test time is reduced.
- The referencing method of the glucose meter is changed from whole blood to blood plasma.

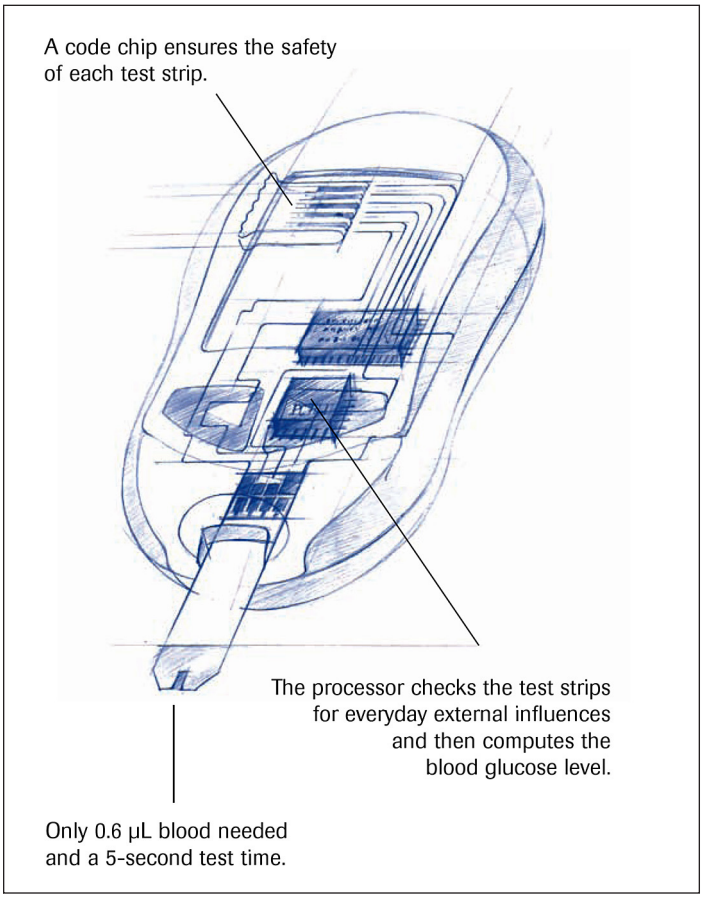

Figure 4. Interaction of the electronic code chip, the processor of the glucose meter, and the glucose test strip in the Roche ACCU-CHEK® Aviva system.

For patients with diabetes, these upgrades offer a clear benefit: they can avail of substantial technological improvements without having to acquire new glucose meters and invest time and effort in learning how to use them. It also significantly reduces the resources needed for retraining diabetes patients, their health care providers, and the diabetes educator teams. The batch-specific code also contains information about the control solution ranges and the expiration date of the glucose test strips. This is a clear advantage for the patient because it significantly enhances the safety of the blood glucose measurement: the glucose meter notifies the user if the expiration date of the test strips is close, so that he or she can replenish the test strips, or automatically rejects test strips that have already expired. This is an important safety feature: if the patient uses expired test strips, the result of the glucose measurement can deviate from the true value and mislead the patient.

The labeling instructions for the Bayer Ascensia® CONTOUR® blood glucose meter are as follows:

> It is important not to use the test strips or control solution if the expiration date printed on the bottle label and carton has passed or it has been six months (180 days) since you first opened the bottle. It will help to write the six month discard date on the label in the area provided when you first open the test strips or control solution. (**Figure 5**)[3]

Figure 5. Glucose test strip bottle of the Bayer Ascensia® CONTOUR® system with handwritten "six month discard date", printed lot number and expiration date.

In other words, Bayer suggests that patients with diabetes write by hand the "six month discard date" on the bottle containing the glucose test strips and stop using them if the discard date has passed. We think that this manual "coding" process is a potential source of error. In real-life situations, patients with diabetes might forget to note the discard date on the bottle, the handwriting might become illegible over time, or the patients might not notice that the discard date has passed. Ultimately, these situations can result in the use of expired glucose test strips.

Conclusions

In summary, coding of glucose test strips offers a broad range of real benefits for patients with diabetes, healthcare providers, and diabetes educators. We believe these benefits largely outweigh having to introduce a glucose test strip code into the glucose meter when a new package of test strips is opened.

Roche's "No Coding" Solution

In Roche's newest all-in-one glucose meter, the ACCU-CHEK Compact Plus system, the coding step for the patient has been eliminated while retaining the benefits described earlier. Technically, this was achieved by integrating the batch-specific code into the drum containing the glucose test strips so that changing the drum means changing the glucose test strip code. As a result, patients using the ACCU-CHEK Compact Plus glucose meter do not have to be concerned about coding.

In the future, further handling steps will be eliminated. For instance, patients will no longer have to discard every single glucose test strip. Instead, used glucose tests will be retained in a cassette until a new cassette is introduced. It is imaginable that the patient with diabetes will only have to place a finger over the glucose meter, and the meter will lance the finger, measure the blood glucose concentration, and indicate the result immediately and automatically. Of course, this glucose meter will retain the safety features of coding without any need for action by the patient.

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Disclosure:

The authors are employees of Roche Diagnostics GmbH, a manufacturer of glucose test strips and meters.

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