Roche Accu-Chek Inform II Strip Lot Metrological Traceability to Higher-Order Reference Material NIST SRM 917 Glucose Powder

The United States Food and Drug Administration (FDA)[i], DIN EN ISO 17511[ii] and Directive 98/79/EC[iii] indicates the reference method, or comparator method, used in manufacturer's performance evaluation of blood glucose monitoring systems (BGMSs) should be traceable to a higher order (e.g., an internationally recognized reference material and/or method). **Figure 1** shows the relationship between the reference material, reference method, and each test lot of Accu-Chek Inform II test strips.

1° Calibrator

The highest-order reference material for glucose is NIST Standard Reference Material (SRM) 917 glucose powder which contains 99.7% +/- 0.3% pure glucose. This NIST SRM 917 glucose powder is used to calibrate the Isotope Dilution Gas Chromatography Mass Spectrometry (ID/GC/MS) reference method.[iv]

2° Calibrator

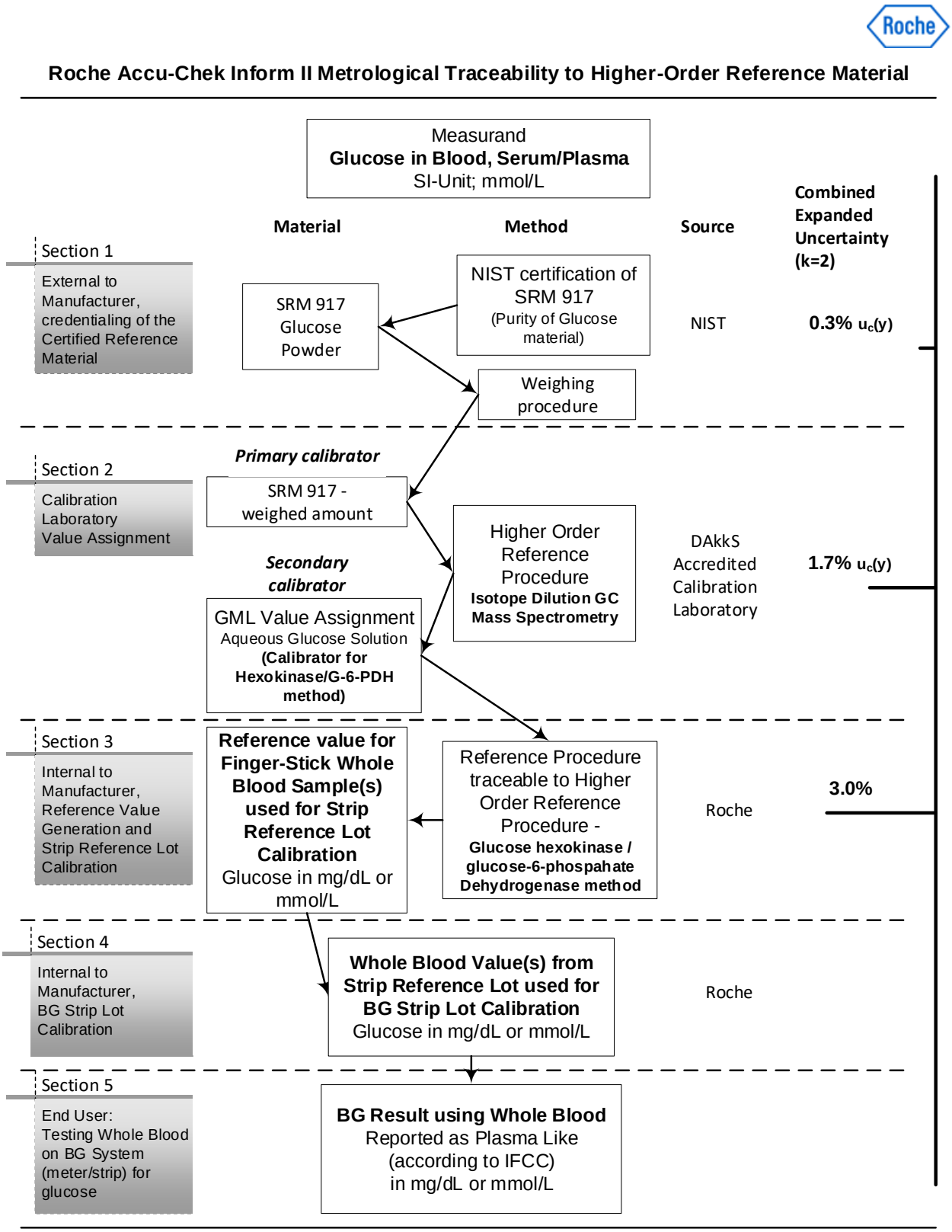
A JCTLM listed, DAkkS accredited calibration laboratory[v] is used to generate via ID/GC/MS the value assignment of the secondary calibrator, an aqueous glucose solution called GML. The GML is then used to calibrate the Roche Diabetes Care's glucose reference method. Capillary whole blood glucose reference samples are prepared and measured on the GML calibrated Roche/Hitachi **cobas c 501** clinical chemistry analyzer utilizing a Hexokinase/G-6-PDH reagent (Glucose-HK). The Reference capillary whole blood glucose concentrations are then converted to plasma estimates in accordance of the IFCC recommendation for reporting glucose results[vi]

3° Calibrator

It is these Reference values that are used to calibrate a Reference Strip Lot by regressing the Reference Lot strip responses to match their respective Reference values. When calibrating Accu-Chek Inform II test strip lots, a Reference Strip Lot serves as the comparator method to obtain the "true" glucose value of a given sample (Code Assignment). This establishes the Reference Strip Lot as a tertiary calibrator that is traceable to the NIST SRM 917 glucose powder.

After Code Assignment, Reference Strip Lot test strips are then run in parallel with the in-process manufacturing Inform II strip lot to determine performance and bias of the Inform II strip lot as part of the strip lot release process (Code Verification).

Figure 1:



[i] FDA Guidance Document, *Blood Glucose Monitoring Test System for Prescription Point-of-Care Use,* issued Oct 2016, p11

[ii] *ISO 17511:2003 In vitro diagnostic medical devices - Measurement of quantities in biological samples - Metrological traceability of values assigned to calibrators and control materials.* ISO 17511 was prepared by the European Committee for Standardization (CEN) in collaboration with Technical Committee ISO/TC 212, Clinical laboratory testing and in vitro diagnostic test systems, in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

[iii] DIRECTIVE 98/79/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 27 October 1998 on in vitro diagnostic medical devices

[iv] White, E., et al., The Accurate Determination of Serum Glucose by Isotope-Dilution Mass-Spectrometry - 2 Methods. Biomedical Mass Spectrometry, 1982. 9(9): p. 395-405. & Jocelyn. L, et al., Modifications to the NIST Reference Measurement Procedure (RMP) for the Determination of Serum Glucose by Isotope Dilution Gas Chromatography/ Mass Spectrometry, Analytical and Bioanalytical Chemistry, 2010, 397(5): P. 1779-1785.

[v] JCTLM (Joint Committee for Traceability in Laboratory Medicine) – international consortium that promotes global standardization of clinical laboratory test results and provides information in reference materials, reference measurement methods and services that are available around the world. DAkkS (Deutsche Akkreditierungsstelle) – National accreditation body for Germany; Calibration Laboratory Accreditation No. D-K-17149-01-00

[vi] IFCC recommendation on reporting results for blood glucose (International Federation of Clinical Chemistry and Laboratory Medicine Scientific Division, Working Group on Selective Electrodes). Clinica Chimica Acta 307 (2001) 205-209