

# Self-Monitoring Blood Glucose Test Systems for Over-the-Counter Use

---

## Guidance for Industry and Food and Drug Administration Staff

Document issued on October 11, 2016.

The draft of this document was issued on January 7, 2014.

For questions regarding this document, contact Leslie Landree at [leslie.landree@fda.hhs.gov](mailto:leslie.landree@fda.hhs.gov), or at 301-796-6147.



U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Devices and Radiological Health  
Office of In Vitro Diagnostics and Radiological Health  
Division of Chemistry and Toxicology Devices

# **Preface**

## **Public Comment**

You may submit electronic comments and suggestions at any time for Agency consideration to <http://www.regulations.gov> . Submit written comments to the Division of Dockets Management, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852. Identify all comments with the docket number FDA-2013-D-1446. Comments may not be acted upon by the Agency until the document is next revised or updated.

## **Additional Copies**

Additional copies are available from the Internet. You may also send an e-mail request to [CDRH-Guidance@fda.hhs.gov](mailto:CDRH-Guidance@fda.hhs.gov) to receive a copy of the guidance. Please use the document number 1756 to identify the guidance you are requesting.

## Table of Contents

I.	INTRODUCTION .....	4
II.	BACKGROUND .....	2
III.	SCOPE.....	3
IV.	REDUCING THE RISK OF BLOODBORNE PATHOGEN TRANSMISSION .....	4
A.	VALIDATED CLEANING AND DISINFECTION PROCEDURES .....	5
B.	DEMONSTRATION THAT THE DEVICE IS ROBUST TO CLEANING AND DISINFECTION PROCEDURES.....	6
V.	DEVICE DESCRIPTION .....	7
VI.	PERFORMANCE EVALUATION AND CRITERIA FOR SMBGS .....	8
A.	PRECISION EVALUATION STUDY .....	9
B.	LINEARITY EVALUATION STUDY.....	10
C.	METHOD COMPARISON/USER EVALUATION .....	11
1.	<i>General Study Design:</i> .....	11
2.	<i>Data Analyses:</i> .....	15
D.	INTERFERENCE EVALUATION.....	15
1.	<i>Endogenous/Exogenous Substances</i> .....	16
2.	<i>Hematocrit</i> .....	18
E.	FLEX STUDIES.....	20
1.	<i>Test Strip Stability Testing</i> .....	22
2.	<i>System Operating Conditions Testing</i> .....	23
3.	<i>Altitude Effects</i> .....	24
4.	<i>Error Codes for Samples Outside the Measuring Range</i> .....	24
5.	<i>Short Sample Detection</i> .....	25
6.	<i>Sample Perturbation Study</i> .....	25
7.	<i>Intermittent Sampling</i> .....	25
8.	<i>Testing with Used Test Strips</i> .....	26
F.	METER CALIBRATION AND QUALITY CONTROL MATERIALS.....	26
VII.	TEST STRIP LOT RELEASE CRITERIA.....	27
VIII.	THIRD PARTY TEST STRIPS.....	28
IX.	SOFTWARE .....	28
X.	LABELING .....	28
	APPENDIX 2. SPECIAL 510(K)S AND SMBGS.....	39

# Self-Monitoring Blood Glucose Test Systems for Over-the-Counter Use

## Guidance for Industry and Food and Drug Administration Staff

*This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.*

### I. Introduction

This guidance document describes studies and criteria that FDA recommends be used when submitting premarket notifications (510(k)s) for self-monitoring blood glucose test systems (SMBGs) which are for over-the-counter (OTC) home use by lay-users.<sup>1</sup> FDA intends for this document to guide manufacturers in conducting appropriate performance studies and preparing 510(k) submissions for these device types.

This guidance is not meant to address blood glucose monitoring test systems which are intended for prescription point-of-care use in professional healthcare settings (e.g., hospitals, physician offices, long term care facilities, etc.). FDA is issuing another guidance entitled “Blood Glucose Monitoring Test Systems for Prescription Point-of-Care Use” (<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM380325.pdf>) to address those device types.

For the current edition of the FDA-recognized standard(s) referenced in this document, see the FDA Recognized Consensus Standards Database Web site at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>.

<sup>1</sup> While the majority of SMBG devices are intended for home use, this also applies to SMBG devices intended for home use that are obtained with a prescription from a healthcare professional.

*Contains Nonbinding Recommendations*

20 FDA's guidance documents, including this guidance, do not establish legally enforceable  
21 responsibilities. Instead, guidances describe the Agency's current thinking on a topic and  
22 should be viewed only as recommendations, unless specific regulatory or statutory  
23 requirements are cited. The use of the word *should* in Agency guidances means that  
24 something is suggested or recommended, but not required.  
25

26 **II. Background**

27  
28 Portable blood glucose meters that measure blood glucose values are used by millions of  
29 people with diabetes every day as an aid in diabetes self-management. These devices are  
30 used by patients in a variety of settings including in their homes, at work, and in schools.  
31

32 Historically, the FDA has not recommended different types of information in premarket  
33 submissions (510(k)s) for blood glucose monitoring systems (BGMSs) intended to be used  
34 by healthcare professionals as compared to SMBGs intended for home use by lay-users.  
35 However, it has become increasingly clear that these different use settings comprise distinct  
36 intended use populations with unique characteristics and different device design  
37 specifications, which manufacturers should take into account when designing their devices  
38 for use in the different intended use populations. Patients in professional healthcare settings  
39 can be acutely ill and medically fragile and are more likely than lay-users to present with  
40 physiological and pathological factors that could interfere with glucose measurements.  
41 Further, the term “lay-user” encompasses a group of individuals with wide ranges in age,  
42 dexterity, vision, training received on performing testing, and other factors that can be critical  
43 in the patient’s ability to accurately use the device and interpret test results. Finally, SMBGs  
44 and the associated test strips used by lay-users are also more likely to experience varied  
45 storage and handling conditions compared to devices used in professional settings. As such,  
46 SMBGs should be designed to be more robust and reliable to accommodate actual use  
47 conditions.  
48

49 In order to distinguish between prescription use blood glucose meters, which are intended for  
50 use in point-of-care professional healthcare settings, and those intended for home use for self-  
51 monitoring by lay-users, the Agency is issuing two separate guidances for (i) BGMSs  
52 intended for use in point-of-care professional healthcare settings, and (ii) SMBGs intended  
53 for home use for self-monitoring by lay-users. The FDA believes that by making this  
54 distinction, SMBGs can be better designed to meet the needs of their intended use  
55 populations, thereby providing greater safety and efficacy.  
56

57 In recent years, concerns have been raised related to infection control issues involving blood  
58 glucose meters and lancing devices. According to the Centers for Medicare and Medicaid  
59 Services (CMS) and the Centers for Disease Control and Prevention (CDC), blood glucose  
60 meters and lancing devices can transmit bloodborne pathogens if these devices are  
61 contaminated with blood specimens and are shared between users without effective cleaning,

## *Contains Nonbinding Recommendations*

62 disinfecting and appropriate infection control measures.<sup>2</sup> Though SMBGs are intended for  
63 home use by lay-users, they should also be designed to withstand effective cleaning and  
64 disinfection procedures over the life of these devices. These disinfection procedures should  
65 be properly validated (see Section IV below) for this type of device and appropriate  
66 instructions provided for the user. Validation methods should take into account the way in  
67 which the device is used, e.g., by lay-users at home (or in other non-professional settings).  
68

### 69 **III. Scope**

70  
71 This guidance document is limited to SMBGs, which are regulated under 21 CFR 862.1345,  
72 Glucose Test System. The product code NBW applies to SMBGs.  
73

74 This document is **not** meant to address the following types of devices:

- 75 • Blood glucose monitoring test systems intended for use in prescription point-of-care  
76 in professional healthcare settings (e.g., hospitals, physician offices, long term care  
77 facilities, etc.).
- 78 • Devices used to screen and diagnose diabetes (such as clinical chemistry analyzers).
- 79 • Continuous glucose sensors, implanted or external (e.g., continuous glucose  
80 monitoring systems (CGMs) or sensors within catheters).
- 81 • Non-invasive glucose measurement devices, (i.e., devices that do not require removal  
82 of a blood sample from a fingertip or other anatomical site).
- 83 • Devices for measurement of blood glucose in neonates.

84  
85 The device types addressed in this guidance document typically use capillary whole blood  
86 from fingertip or alternative anatomical sites. These device types are not intended for use in  
87 healthcare or assisted-use settings such as hospitals, physician offices, or long-term care  
88 facilities because they have not been evaluated for use in these professional healthcare  
89 settings, including for routine assisted testing or as part of glycemic control procedures. Use  
90 of these devices on multiple patients may lead to transmission of Human Immunodeficiency  
91 Virus (HIV), Hepatitis C Virus (HCV), Hepatitis B Virus (HBV), or other bloodborne  
92 pathogens.

93  
94 While FDA recommends that the information described in this guidance be included in  
95 premarket submissions for SMBGs, submissions containing alternative information may be  
96 sufficient if able to demonstrate substantial equivalence to a legally marketed predicate  
97 device.  
98

99 We recommend that you contact the Division of Chemistry and Toxicology Devices in the  
100 Office of In Vitro Diagnostics and Radiological Health if you have questions regarding  
101 alternate intended uses of your SMBG.

---

<sup>2</sup> See information at <http://www.cdc.gov/injectionsafety/blood-glucose-monitoring.html>.

102  
103

104 **IV. Reducing the Risk of Bloodborne Pathogen**  
105 **Transmission**

106

107 Since SMBGs use blood specimens for glucose measurement, their design and instructions  
108 for use are very important factors in reducing the risk of bloodborne pathogen transmission  
109 during use. According to the Centers for Medicare and Medicaid Services (CMS) and the  
110 Centers for Disease Control and Prevention (CDC), blood glucose meters, as well as lancing  
111 devices, can transmit bloodborne pathogens, such as viral hepatitis, if these devices are  
112 contaminated with blood specimens and are shared between users without effective cleaning  
113 disinfecting, and appropriate infection control measures. To minimize the risk of bloodborne  
114 pathogen transmission with single patient use SMBGs, you should address the following in  
115 your device’s design and labeling:  
116

- 117 • All SMBGs should be intended for single patient use. The intended use should  
118 clearly state that the SMBG is intended for home use by lay-users and should only be  
119 used on a single user.
- 120 • Meters should be designed such that all external materials can be cleaned (removal of  
121 organic soil) and disinfected (microbicidal process).
- 122 • All external surfaces of the meter, including seams and the test strip port, should be  
123 designed for both ease of use and ease of cleaning and disinfection.
- 124 • You should develop an effective disinfection method that can be easily employed by  
125 lay-users at home. You should provide the validated cleaning and disinfecting  
126 procedures for your SMBG in your 510(k) submission as well as in the labeling.  
127 Cleaning and disinfection are different processes and need separate validation  
128 procedures and specifications. See Sections IV.A and B. below for details on the  
129 recommended cleaning and disinfecting validation studies.
- 130 • You should validate the efficacy of any disinfectant you recommend for use with your  
131 device, as described below. We recommend you consult the Environmental  
132 Protection Agency’s (EPA) list of disinfectants that are registered for use against  
133 infectious bacteria and viruses<sup>3</sup> when choosing disinfectants to validate for use with  
134 your device.
- 135 • You should clearly warn users that lancing devices are for single-patient use only and  
136 should NEVER be shared.
- 137 • Labeling concerning safe device use can reduce the risk of user error; therefore,  
138 instructions for cleaning and disinfection should be clear and detailed. The various  
139 test system components should be named in such a way that they are recognized as  
140 belonging to the same system or family of products, and to distinguish them from  
141 similar devices intended for multiple-patient use (e.g., ABC blood glucose test

---

<sup>3</sup> Selected EPA-registered Disinfectants <http://www.epa.gov/oppad001/chemregindex.htm>

*Contains Nonbinding Recommendations*

142 system, ABC blood glucose meter, ABC blood glucose test strips, etc.). See Section  
143 X, Labeling below for detailed labeling recommendations.

144

145 Validation of cleaning and disinfection procedures involves both validation that the cleaning  
146 and disinfection products are effective against the primary viruses of concern (i.e., HIV,  
147 Hepatitis B, Hepatitis C) and validation that the cleaning and disinfection procedures do not  
148 deteriorate the device or alter device performance. FDA’s recommendations for such  
149 validation are outlined in the following sub-sections.

150

151 ***A. Validated cleaning and disinfection procedures***

152

153 You should select cleaning and disinfection products that do not result in physical  
154 deterioration of the device overall, or any device component including the housing,  
155 touch pad, or buttons. You should make note of any physical indicators of deterioration  
156 during your validation study and provide this information in your 510(k) submission.

157 The disinfectant product you choose should be effective against HIV, Hepatitis C, and  
158 Hepatitis B viruses. Of these viruses, Hepatitis B is the most difficult to kill and prior  
159 outbreak episodes associated with blood glucose meters have been due to transmission  
160 of Hepatitis B viruses. Therefore, disinfection efficacy studies should be performed to  
161 demonstrate effectiveness of the chosen disinfectant against Hepatitis B virus. Please  
162 note that 70% ethanol solutions are not effective against viral bloodborne pathogens,  
163 and the use of 10% bleach solutions may lead to physical degradation of your device.

164

165 You should demonstrate that your disinfection procedure is effective against Hepatitis B  
166 virus by performing disinfection efficacy studies to show that your procedure is effective  
167 with the external meter materials (e.g., case, display, buttons, etc.). Studies have  
168 demonstrated that viruses can remain infective for different time periods, depending on  
169 the surface. Viral survival may increase or decrease with the number of microbes present  
170 on a surface. Increasing amounts of microbes can protect viruses from disinfection and  
171 damaging effects may also result from microbial proteases and fungal enzymes. Factors  
172 that influence survival on surfaces include fomite properties, initial viral titer, virus strain,  
173 temperature, humidity and suspending media. The simplest disinfection method would  
174 be the use of towelettes pre-saturated with a selected disinfectant. Disinfection with a  
175 towelette will reduce the risk of liquid getting into the meter, thereby minimizing the  
176 chance of your disinfection procedure affecting meter function. However, you should  
177 choose a disinfectant that is effective against Hepatitis B Virus and is compatible with  
178 your specific device. If you intend to claim that your disinfection procedure is effective  
179 against other pathogens you should consider submitting a pre-submission request to  
180 discuss this with the Agency prior to conducting your testing. For information about the  
181 pre-submission process, see FDA’s guidance entitled “Requests for Feedback on Medical  
182 Device Submissions: The Pre-Submission Program and Meetings with Food and Drug  
183 Administration Staff

184 <http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidanced>



## *Contains Nonbinding Recommendations*

185 [ocuments/ucm311176.pdf](#)). In addition, you should choose a disinfection method that  
186 uses products that would be readily available to the home user.

187  
188  
189 We recommend you refer to the following standards:

- 190 • ASTM standard ASTM E1053-11, Standard Test Method for Efficacy of  
191 Virucidal Agents Intended for Inanimate Environmental Surfaces
  - 192 • ASTM standard ASTM E2362 -09, Standard Practice for Evaluation of Pre-  
193 saturated or Impregnated Towelettes for Hard Surface Disinfection.
- 194

### ***B. Demonstration that the device is robust to cleaning and disinfection procedures***

195  
196

197  
198 You should demonstrate through bench studies that your SMBG is robust to cleaning and  
199 disinfection procedures after multiple cleaning and disinfection cycles. You should  
200 include in your 510(k) submission the study design and results demonstrating that the  
201 analytical performance of the SMBG is not impacted by the cleaning and disinfection  
202 procedures.

203  
204 You should address the following in designing your study:

- 205  
206 • You should choose worst case scenarios with regards to cleaning and disinfection  
207 frequency and end user environment to determine the number of cleaning and  
208 disinfection cycles that should be tested. For example, the number of times you clean  
209 and disinfect the meter should be representative of the cleaning and disinfection that  
210 the meter will be exposed to during its use life (typically 3-5 years) and may be  
211 greater than the number of cleaning and disinfection cycles recommended in the user  
212 instructions. A cleaning step should precede the disinfection step for each cleaning  
213 and disinfection cycle.
- 214 • The disinfection contact time used in the robustness study should be identical to the  
215 contact time used in the disinfection efficacy testing and described in the cleaning and  
216 disinfection instructions in the labeling.
- 217 • We recommend using the same disinfectant product for both cleaning and  
218 disinfection. The effects of multiple products on the efficacy of the disinfectant  
219 products are not well understood.
- 220 • You should demonstrate that the test strip port and all other openings that are  
221 susceptible to blood contamination and could either directly or indirectly be contacted  
222 by the user are able to withstand your recommended cleaning and disinfection  
223 procedures. You should ensure that you test parts of the meter that are particularly  
224 susceptible to blood contamination, such as the test strip port and any material seams.  
225 It is important to be able to clean and disinfect all parts of your meter to reduce the  
226 risk of bloodborne pathogen transmission.

*Contains Nonbinding Recommendations*

- 227
- 228
- 229
- 230
- 231
- 232
- 233
- 234
- 235
- 236
- 237
- When you evaluate your device after the cleaning and disinfection phase, you should ensure that the procedure does not cloud or deface the display of the meter and does not corrode or erode the plastic housing or buttons. You should note all physical indicators of deterioration throughout your study and you should include these results in your 510(k) submission. You should evaluate the accuracy of the meter using blood samples compared to results obtained by a comparator method (please refer to Section VI below for the definition of comparator method) to ensure that accuracy is not affected by repeated cleaning and disinfection. You should also evaluate the functionality of your meter features (as appropriate), for example, touch screen function, USB port function, speaking functions, etc., to ensure they are not affected by repeated cleaning and disinfection.
  - You should include infection control in your risk analysis and incorporate your validated cleaning and disinfecting procedures into your risk assessment.
- 238
- 239

240

241 You should include a description of the protocols and acceptance criteria for all studies in

242 your 510(k) submission.

243

244 **V. Device Description**

245

246 You should provide a general description of the SMBG in your 510(k) submission. Typically,

247 much of this information should also be included in the device’s User Manual; however,

248 some of the information is not appropriate for the intended lay-user (e.g., highly technical

249 explanations) and should be included in the 510(k) submission only. You should provide the

250 following in your 510(k) submission.

251

252 General device description:

- 253
- Description of physical components of the system (including diagrams where
    - appropriate).
  - Manufacturer’s performance specifications.
  - Description and explanation of the test principle, including chemical reactions.
  - Description of the format of results, including units of measurement and whether results are reported in whole blood or plasma equivalents.<sup>4</sup>
  - Description of the composition and levels of control material that can be used with your system.
  - User maintenance needs (e.g., batteries).
  - Features of the device, such as data transmission capabilities or features designed to enhance robustness and ease of use.
  - Features designed to minimize the risk of bloodborne pathogen transmission.
- 254
- 255
- 256
- 257
- 258
- 259
- 260
- 261
- 262
- 263
- 264
- 265

---

<sup>4</sup> Note that SMBGs intended for use in the U.S. should report results in mg/dL and in plasma equivalents.

## *Contains Nonbinding Recommendations*

266  
267  
268  
269  
270  
271  
272  
273  
274  
275  
276  
277  
278  
279  
280  
281  
282  
283  
284  
285  
286  
287  
288  
289  
290  
291  
292  
293  
294  
295  
296  
297

Description of features controlled by the software, which should describe the following:

- Displays and user messages: This includes how the SMBG determines and displays the glucose concentration, messages or displays that appear while a user is taking a measurement, and features such as how a user can retrieve past results from storage in the device.
- User prompts: You should describe prompts that the SMBG provides to the user, expected user responses, and timing issues (e.g., how quickly does the user need to respond, what happens if they respond after the allowed time). Examples of user prompts include messages to the user to insert the test strip into the meter, add blood sample to the test strip, calibrate the meter, or store a result, etc.
- Error messages and alerts: This includes any error messages or alerts that the SMBG displays. You should describe how the system responds to errors in user action, user inaction, or system status. Suggested examples of error messages or alerts include when a strip is inserted incorrectly or removed prematurely, too small a sample is applied to the test strip, damaged, incorrect or deteriorated strips are used, or when there is a low battery or excessively high ambient temperature. You should also include the methods by which the SMBG detects and alerts the user when glucose levels are outside of the linear range of the system. You should describe at what point each message is triggered and describe any self-diagnostic routines that the system performs.

It is important that you identify the expected responses by the user to error messages or alerts. This includes whether and how the user should input information or press certain buttons to correctly set up the meter or to respond to an error message or alert.

## **VI. Performance Evaluation and Criteria for SMBGs**

298  
299  
300  
301  
302  
303  
304  
305  
306  
307  
308

Subsections A-F below indicate the types of device performance information that you should include in a 510(k) submission for a SMBG. Although many manufacturers design their SMBG validation studies based on the International Standards Organizations document 15197: “In vitro diagnostic test systems—Requirements for blood glucose monitoring systems for self-testing in managing diabetes mellitus,” FDA believes that the criteria set forth in the ISO 15197 standard are not sufficient to adequately protect lay-users using SMBGs; therefore, FDA recommends performing studies to support 510(k) clearance of a SMBG according to the recommendations below.

*Contains Nonbinding Recommendations*

309 In this guidance, the term “comparator method” refers to a laboratory-based glucose  
310 **measurement method that has been well-validated for precision and accuracy** and that is  
311 traceable to a higher order, e.g., an internationally recognized reference material and/or  
312 method. The traceability chain should include as few stages as possible to reduce bias.  
313 FDA’s current thinking on the issues that should be addressed and the recommended study  
314 designs and device performance evaluations are discussed below in Subsections A-F.  
315

316 **A. Precision Evaluation Study**

317 You should evaluate both within-run precision and intermediate precision for your SMBG  
318 and include these evaluations in your 510(k) submission. The following outlines FDA’s  
319 current thinking on appropriate study design and analyses to evaluate within-run precision  
320 and intermediate precision for SMBGs.

321

322 *Within-Run Precision Evaluation:*

323 Within-run precision studies are bench studies designed to evaluate imprecision under  
324 conditions of repeated measurement of the same sample with different meters and  
325 multiple test strip lots. In order to assess imprecision of the SMBG across the claimed  
326 measuring range, you should evaluate samples containing glucose concentration within  
327 each of the five intervals provided in Table 1 below:  
328

329

**Table 1. Glucose Concentrations for Precision Evaluation**

<b>Interval</b>	<b>Glucose Concentration Range (mg/dL)</b>
1	30-50
2	51-110
3	111-150
4	151-250
5	251-400

330

331 You should determine within-run precision using venous whole blood samples. Altered  
332 venous whole blood samples such as those that are spiked, diluted, or allowed to  
333 glycolyze in order to obtain the appropriate glucose concentrations are acceptable in order  
334 to facilitate coverage of the entire claimed glucose measuring range. However, you  
335 should clearly identify all altered samples (spiked, diluted, or glycolyzed) in all submitted  
336 data. A minimum of 500 test strips from at least 10 vials and 3 manufacturing lots should  
337 be used in this study. For each sample concentration, a minimum of 10 meters should be  
338 used, with at least 10 measurements taken by each meter (i.e., at least 100 measurements  
339 per concentration). Test strips should be taken from the same vial and/or package for each  
340 meter.  
341

342

343 We recommend you present the results as the mean value of all measurements per meter  
344 for each glucose concentration range with the corresponding standard deviation (SD) and  
345 percent coefficient of variation (CV). In addition, for each glucose concentration range in  
Table 1, you should also provide the mean value, standard deviation (with 95%

## *Contains Nonbinding Recommendations*

346 confidence intervals) and percent CV for data combined over all meters. You should  
347 describe the statistical procedures used in the analysis.

348

349 You should provide the results based on all data; if any outlier samples were excluded  
350 from any of your statistical analyses, you should fully describe the method of outlier  
351 identification, identify the excluded samples, and provide the results of your root cause  
352 investigations into the outlier samples.

353

354 *Intermediate Precision Evaluation:*

355 Intermediate precision measurement studies are bench studies designed to evaluate  
356 imprecision under simulated normal use conditions, for example, measurement over  
357 multiple days using multiple reagent system lots. These studies may be performed with  
358 prepared control solutions rather than whole blood samples.

359

360 The total number of meters and operators in these studies is at the discretion of the  
361 sponsor; however, a minimum of 10 meters should be used for each glucose  
362 concentration. Intermediate precision should be evaluated over a minimum of 10 days,  
363 taking at least 1 measurement per meter per day of a sample from each glucose  
364 concentration interval listed in Table 1. This should produce a minimum of 10  
365 measurements per meter for each glucose concentration and 100 total measurements per  
366 glucose concentration. You should use a minimum of 500 test strips from a minimum of  
367 10 vials or packages that cover a minimum of 3 manufacturing lots. These test strips  
368 should be taken from the same vial and/or package for each meter.

369

370 For each glucose concentration in Table 1, you should present data for each test strip lot  
371 and also for pooled lots including the mean value of the measurements for each meter  
372 with the corresponding standard deviation (SD) and percent coefficient of variation (CV).  
373 You should also present the mean value, standard deviation (with 95% confidence  
374 intervals) and percent CV for data combined over all meters. You should describe the  
375 statistical procedures you use. You should provide results based on all data; if any outlier  
376 samples were excluded from any of your statistical analyses, you should fully describe the  
377 method of outlier identification, identify the excluded samples, and provide the results of  
378 your root cause investigations into the outliers.

379

### 380 ***B. Linearity Evaluation Study***

381 You should evaluate the linearity of your device across the entire claimed measuring  
382 range. We recommend that studies include an evaluation of at least 11 evenly spaced  
383 concentrations tested and analyzed according to “Evaluation of the Linearity of  
384 Quantitative Measurement Procedures: A Statistical Approach”, CLSI document EP6-A.  
385 Linearity studies should be performed using venous whole blood samples. Altered  
386 venous whole blood samples, such as those that are spiked, diluted, or glycolyzed are  
387 acceptable in order to facilitate coverage of the entire claimed measuring range. You  
388 should clearly identify the number of altered samples (spiked, diluted, or glycolyzed)  
389 within the 510(k) submission.

*Contains Nonbinding Recommendations*

390  
391  
392  
393  
394  
395

You should submit a detailed description of the study design, target concentrations, a list of all data collected in this study, summary of the results and conclusions drawn from the study, and a description of the statistical analysis used.

396 ***C. Method Comparison/User Evaluation***

397  
398

**1. General Study Design:**

399  
400  
401  
402  
403  
404

We recommend that you design a single evaluation to assess both system accuracy in the hands of the intended users as well as other aspects to support lay-use, such as a labeling assessment and usability. This type of design will more accurately reflect the device performance in the hands of the intended user, thereby providing a better estimate for total accuracy of your SMBG.

405  
406  
407  
408  
409  
410  
411  
412  
413  
414  
415

FDA recognizes that most study evaluations performed for 510(k) submissions occur in idealized conditions, thereby potentially overestimating the total accuracy of the SMBG, even when performed in the hands of the intended user. It is important to design your study to most accurately evaluate how the device will perform in the hands of the intended use population. Therefore, the study should be conducted under conditions that reflect the expected use of the device by the intended use population (e.g., temperature, humidity, altitude, etc.), but does not need to be conducted across the entire range of environmental conditions (environmental conditions are validated separately in Flex Studies discussed in Section VI.E below). You should fully describe the conditions of your study in your 510(k) submission.

416  
417  
418  
419  
420  
421  
422  
423  
424

You should include at least 350 different subjects in your user evaluation. More than one comparator measurement may be taken and averaged for each sample in order to allow a better estimate of the true glucose value of that sample. However, no measurements should be excluded from the data analysis. If you are planning to include claims that your device can be used at alternative anatomical sites (e.g., forearm, palm, etc.), you should test samples using your device from 350 subjects for each alternative anatomical site for which you are seeking clearance and evaluate the results relative to samples measured with the comparator method.

425  
426  
427  
428  
429  
430  
431  
432  
433

For each claimed anatomical site, the samples should adequately span the claimed measuring range of the SMBG. Though it may be difficult to obtain samples at the extreme ends of the measuring range, the study should contain at least 10 unaltered samples with blood glucose concentrations < 80 mg/dL, and at least 10 unaltered samples between 250 mg/dL glucose and the upper limit of the claimed measuring range of the device. It may be necessary to enroll more than 350 patients for each anatomical site (fingertip, forearm, palm, etc.) in order to obtain at least 10 unaltered samples < 80 mg/dL and at least 10 unaltered samples between 250mg/dL and the upper limit of the claimed measuring range of the device. Data from all subjects in the study should be submitted in

### *Contains Nonbinding Recommendations*

434 your 510(k) (even if more than 350 samples are collected), and no subjects should be  
435 excluded from the data analysis.

436

437 The subjects you enroll in the method comparison/user study should accurately reflect the  
438 intended use population of the SMBG. The study group should be comprised of both  
439 naïve and non-naïve SMBG users. At least 10% of the study participants should be naïve  
440 to SMBGs and may include non-diabetic subjects. You should describe the inclusion and  
441 exclusion criteria for enrolling the study participants, as well as the demographic  
442 characteristics of the subjects that participated in the study.

443

444 Prior to testing, study subjects should be given the draft device labeling (instructions for  
445 use, user manual, etc.) that is representative of the labeling that will be provided to the  
446 user with the marketed device. If major revisions are made to the labeling after the user  
447 evaluation has concluded, an additional user study may be indicated if there is no other  
448 method available to validate that the changes made do not affect user performance. For  
449 purposes of the study, the instructions for use should be written in English only;  
450 translations into other languages should not be provided to study participants. Prior to  
451 the study, you should perform a readability assessment (in terms of grade level) of the  
452 user manual, test strip insert, and control solution insert. For a product intended for  
453 home use by lay-users, the reading level should be at an 8<sup>th</sup> grade level or less. We  
454 recommend using the Flesch-Kincaid, SMOG, or equivalent computer program to  
455 assess the readability grade level of the labeling. You should describe the assessment  
456 and results in your 510(k) submission.

457

458 The study subjects should obtain their own fingertip capillary (or alternate anatomical  
459 site(s)) sample and perform a blood glucose test using only the draft device labeling as  
460 instructions. No other training or prompting should be provided to the user, and they  
461 should not receive assistance from a study technician or healthcare provider to obtain the  
462 test result. Study subjects should be sequestered in such a way that they cannot observe  
463 or be influenced by the testing technique of other study participants or technicians. Once  
464 the study participant has obtained their own result using the SMBG, the technician should  
465 then obtain an additional capillary sample for testing using the comparator method. Since  
466 the intended user population of SMBGs is the lay-user, it is not necessary for the  
467 technician to obtain capillary results on the SMBG for comparison to the comparator  
468 value.

469

470 In the study, you should include a minimum of 10 test strip vials or packages that cover a  
471 minimum of 3 test strip lots. All test strips used in the study should have undergone  
472 typical shipping and handling conditions from the site of manufacture to a U.S. user prior  
473 to being used in the study. You should describe these shipping and handling conditions  
474 in your 510(k) submission.

475

476 Hematocrit values should be determined and recorded for each of the study participants.  
477 You should present individual hematocrit values in the 510(k) submission along with the  
478 meter results.

## *Contains Nonbinding Recommendations*

479  
480  
481  
482  
483  
484  
485  
486  
487  
488  
489  
490  
491  
492  
493  
494  
495  
496  
497  
498  
499  
500  
501  
502  
503  
504  
505  
506  
507  
508  
509  
510  
511  
512  
513  
514  
515  
516  
517  
518  
519  
520  
521  
522  
523

Blood glucose test results are used by people with diabetes to make critical decisions about their treatment; therefore, it is important that the results are accurate so that nutritional and drug dosing errors are better avoided. Your studies should demonstrate that your SMBG is sufficient for this purpose by showing that 95% of all SMBG results in this study are within +/- 15% of the comparator results across the entire claimed measuring range of the device and that 99% of all SMBG results are within +/- 20% of the comparator results across the entire claimed measuring range of the device. You should include all results in the 510(k) submission. Though we expect that with the technologies available, SMBG devices will be able to meet this criteria, there may be instances where meters may be determined to be substantially equivalent even when performance does not meet these criteria because, for example, other features of the meter or its setting of use provide benefits that compensate for different performance. For all SMBG test results that are >20% relative to the comparator method, you should provide a clinical justification for why the errors occurred and describe why the potential for that error does not affect user safety when extrapolated to the intended use setting (e.g., when billions of tests are performed). We will review any submitted justification to determine whether the data suggest that patients may be put at risk, or whether the justification and any proposed mitigation are adequate.

FDA understands that some SMBGs may not be able to measure reliably within 15% of the comparator method at very low glucose concentrations. If this is the case, you should raise the lower end of the claimed measuring range to the concentration where your device is sufficiently accurate according to the above described criteria. To meet the clinical needs of the user population, SMBGs should minimally be able to measure blood glucose accurately between 50 mg/dL and 400 mg/dL, or a clinical justification should be provided for alternate measuring ranges. A SMBG should identify and provide an error code in situations where the measured glucose value falls outside of the device's stated measuring range. For example, meter XYZ has a measuring range that can detect glucose concentrations down to 50 mg/dL; therefore, blood samples with glucose concentrations below 50 mg/dL should provide an appropriate error code (e.g., "LOW - Less than 50 mg/dL").

Method comparison and user performance studies for a SMBG should include multiple blood glucose meters being used amongst the 350 lay-user study participants. Individual lancing devices should be used for each subject and meters should be cleaned and disinfected using validated instructions during the course of this study. You should provide procedures to mitigate the risk of potentially transmitting disease between healthcare providers and subjects during the study (for example, use of disposable gloves or other physical barriers), including details on how often and when gloves worn by the trained health professionals should be changed between subjects. Refer to Section IV above (Reducing the Risk of Bloodborne Pathogen Transmission in Diabetes Care) for additional information regarding the validation of cleaning and disinfecting of SMBGs. You should describe these aspects of the study in your 510(k) submission.



## *Contains Nonbinding Recommendations*

524  
525  
526  
527  
528  
529  
530  
531  
532  
533  
534  
535  
536  
537  
538  
539  
540  
541  
542  
543  
544  
545  
546  
547  
548  
549  
550  
551  
552  
553  
554  
555  
556  
557  
558  
559  
560  
561  
562  
563  
564  
565

You should also describe the following in your 510(k) submission:

- Study setting including the size, type, and location of each site and a justification of how the selected study conditions simulate intended use conditions. Study sites should be representative of where SMBGs are used in the U.S. and you should include an explanation of why you believe each site is representative of where SMBGs are used.
- Criteria used to select study subjects, including inclusion and exclusion criteria. Patient demographics (age range, education level, native language, laboratory or healthcare work experience, disease state) and whether they are a naïve SMBG user or not.
- Details of procedures performed by lay-users and study technicians.
- Instructions provided to users in the study. (Note: All instructions should be provided to users in English only.)
- Type of sample collected (anatomical collection site(s)).
- Number of test strip lots, number of test strip vials, and number of meters used in the study.
- Description of the shipping and handling conditions of the test strips prior to use in the study.
- A user questionnaire should be provided for the study participants to fill out after completing the study. A copy of the blank questionnaire and the analysis of the results should be provided in the 510(k) submission.

### *Accuracy at Extreme Glucose Values*

Because the user study described above using real patient samples may not provide a robust evaluation of SMBG performance in the extreme upper and lower ends of the claimed measuring range, you should perform additional studies using blood samples altered to achieve glucose concentrations of less than 80 mg/dL and greater than 250 mg/dL. These samples should mimic unaltered patient samples as closely as possible. This additional extreme glucose value study should be performed separately from the user study (see Section VI.C) described above and may be performed in a laboratory setting.

Capillary whole blood samples should be used for these studies; a professional may need to collect the capillary blood to ensure the sample size is sufficient. You should include a minimum of 50 prepared samples containing glucose concentrations below 80 mg/dL and 50 samples greater than 250 mg/dL. These samples should evenly cover the lower and upper limits of the claimed measuring range. Samples may be altered by spiking or allowing the samples to glycolyze in order to obtain the appropriate glucose concentrations. Samples should be measured on both the SMBG and the comparator method. You should analyze these data separately from the user

## Contains Nonbinding Recommendations

566 evaluation data but using the same methods described below for the user evaluation  
567 studies. FDA will apply the same review criteria to both studies.

568

### 569 **2. Data Analyses:**

570 *Data exclusion and outliers:*

571 You should present all data in the 510(k) submission, including cases in which the meter  
572 displays an error code, a 'High' or 'Low' message, or no result. All outliers (e.g., data  
573 points that do not conform to the minimum accuracy criteria) should also be included.

574 You should investigate all outlier results and describe the results of these investigations,  
575 providing explanations for the occurrence of outliers when possible. To help inform your  
576 investigations into outlier results, you should collect information regarding patient  
577 medications, hematocrit measurements and disease states during your study.

578

579 *Analysis of results:*

580 You should present the difference between individual study subject results and results of  
581 the comparator method (or mean of the comparator measurement, if multiple replicates  
582 are measured on the comparator method) by plotting the data on an X-Y graph. The plot  
583 should include the regression line and line of identity, as well as the 99% confidence  
584 regions for the regression prediction. Your summary of results should include the slope  
585 and y-intercept, calculated using a suitable analysis procedure (e.g., Linear Regression,  
586 Deming Regression), and the estimate of the deviation (standard error). Bland-Altman  
587 analysis may also be presented. You should describe all statistical methods used and  
588 clearly identify and describe any outliers in the analysis.

589

590 *Tabular data presentation:*

591 You should present the results of regression analysis in the following tabular format for  
592 each sample matrix. In Table 2 below, X= the number of samples within the specified  
593 difference from the comparator method, and Y= total number of samples.

594

595 **Table 2. Summary of data within specified mg/dL of the comparator method for**  
596 **glucose concentrations across the entire range:**

Within +/- 5%	Within +/- 10%	Within +/- 15%	Within +/- 20%
X/Y (%)	X/Y (%)	X/Y (%)	X/Y (%)

597

### 598 **D. Interference Evaluation**

599

600 You should evaluate the effect of potentially interfering endogenous and exogenous  
601 substances and conditions such as icterus, lipemia, and varying hematocrit levels, as well  
602 as the effect of common medications on your SMBG's performance. Conditions that are  
603 known to interfere with glucose monitoring test systems, such as ketoacidosis, should be  
604 included in the labeling as limitations. If you would like the labeling to not include these  
605 limitations or if you would like to remove these conditions from the labeling, you should  
606 provide interference testing demonstrating that these conditions do not interfere with your  
607 device.

## Contains Nonbinding Recommendations

608

609

### 610 **1. Endogenous/Exogenous Substances**

611

#### *Study design:*

612 You should perform interference testing using samples containing glucose concentrations  
613 across the range of the device. Specifically, testing should be performed in samples with  
614 target glucose values of approximately 50 - 70 mg/dL, 110-130 mg/dL, and 225-270  
615 mg/dL to evaluate clinically relevant decision points.

616

617 You should evaluate each potentially interfering substance at clinically relevant  
618 concentrations, and should test all substances at the highest concentration that could  
619 potentially be observed in a whole blood sample; if significant interference is observed,  
620 you should perform dilutions of the interferent to determine the concentration at which  
621 interference begins to occur. For example, if interference is observed with 20 mg/dL  
622 acetaminophen, additional testing should be performed with samples containing lower  
623 concentrations of acetaminophen, such as 15 mg/dL, 10 mg/dL and 5 mg/dL, to determine  
624 the lowest concentration of acetaminophen where interference is first observed. If the  
625 results from the additional testing determine that interference is not observed in the  
626 sample containing 5 mg/dL acetaminophen and interference is observed in the sample  
627 containing 10 mg/dL acetaminophen, then 10 mg/dL is the lowest concentration of  
628 acetaminophen where interference begins to occur.

629

630 The substances listed below in Table 3 below represent known or potential interferents  
631 for current blood glucose measurement technologies and comprise the minimal list of  
632 substances that should be tested for interference.

633

634

**Table 3. List of Known or Potential Interferents for SMBGs.**

<b>Interferent</b>	<b>Recommended Test Concentration</b>
Acetaminophen	20 mg/dL
Ascorbic acid	3 mg/dL
Conjugated Bilirubin	50 mg/dL
Unconjugated Bilirubin	40 mg/dL
Cholesterol	500 mg/dL
Creatinine	10 mg/dL
Dopamine	20 mg/dL
EDTA*	200 mg/dL
Galactose	15mg/dL
Gentisic acid	1000 mg/dL
Reduced Glutathione	92 mg/dL
Hemoglobin	20 g/dL
Heparin*	500 IU/dL

### *Contains Nonbinding Recommendations*

Ibuprofen	50 mg/dL
Icodextrin	1094.4 mg/dL
L-Dopa	0.5 mg/dL
Maltose	10,000 mg/dL
Methyldopa	1000 mg/dL
Salicylic acid	60 mg/dL
Sodium	414 mg/dL
Tolbutamide	100 mg/dL
Tolazamide	40 mg/dL
Triglycerides	1500 mg/dL
Uric acid	24mg/dL
Xylose	200 mg/dL
Sugar Alcohols**	0.09 mg/dL

635 \*The inclusion of EDTA and Heparin in this table refers to their use as therapeutic substances and not as  
636 anticoagulants for sample preparation.

637 \*\*All common sugar alcohols, including but not necessarily limited to, mannitol, sorbitol, xylitol, lactitol,  
638 isomalt, maltitol should be independently tested.

639

640 In addition to the list of potential interferents provided in Table 3, you should conduct an  
641 interference risk analysis and carry out bench studies to evaluate interference from  
642 additional drugs commonly used in your intended use population.

643

644 You should provide a reliable estimate of the interference predicted for each potential  
645 interferent. To do this, we recommend the following method of measuring and  
646 calculating interference. First, blood samples should be generated at each target glucose  
647 concentration described above. Each glucose sample should be tested in replicates with  
648 the comparator method (we suggest at least 4 replicates in order to reduce standard error)  
649 to establish the glucose concentration in the sample. The glucose samples should then be  
650 split into a test sample to which a specific amount of potential interferent is added and a  
651 control sample containing solvent/vehicle in lieu of the potential interfering substance.  
652 Both control samples and test samples should be measured in replicates on the SMBG.  
653 At least three test strip lots should be used for this evaluation. Each of the control and test  
654 samples should be tested on your SMBG in replicates of 30 across the three lots (10  
655 replicates per lot of test strips for a total of 30 replicates per sample). The mean of  
656 replicates should be calculated for each control and test sample. The relative bias (mg/dL)  
657 and percent bias should be calculated using the results of the control sample relative to  
658 test sample for each concentration of potential interferent. These results should be  
659 submitted with 95% confidence intervals as part of your 510(k) submission.

660

661 For SMBGs, the degree of acceptable interference may vary by substance tested and the  
662 intended patient population of your device. Therefore, you should report in your 510(k)  
663 submission the interference testing data as well as the expected imprecision of the system  
664 at that glucose concentration. If interferences are observed, you should propose  
665 appropriate labeling to address any observed interferences; the labeling language  
666 appropriate for the observed interference will be discussed during the review of the  
667 510(k) submission.

## Contains Nonbinding Recommendations

668

669 As new drugs are developed that could potentially interfere with your device, or new  
670 interfering substances are identified for other SMBGs, you should evaluate these new  
671 drugs or substances for potential interference with your device. For example, if a new  
672 drug intended to treat cardiac complications in diabetic patients is approved, you should  
673 conduct a careful evaluation to determine whether the new drug interferes with your  
674 device. You should report to FDA if significant new interferences are observed with your  
675 device or with any cleared glucose monitoring devices that are on the market. New  
676 drugs/potential interferents should also be evaluated when new or significantly modified  
677 technology is introduced.

678

679 *Data Analysis:*

680 You should provide raw data sets as well as a summary table for all interference results.  
681 Please note that the summary tables should be presented separately for each test strip lot  
682 and for all lots pooled for each glucose level tested. Table 4 below provides a sample  
683 format of a summary table.

684

685 **Table 4. Recommended Summary Table Format:**

686

*Test Strip Lot #(s)*

<b>Interferent</b>	<b>Mean Glucose Value (Comparator)</b>	<b>Interferent Concentration (mg/dL)</b>	<b>Control Sample Mean</b>	<b>Test Sample Mean</b>	<b>Bias (mg/dL)</b>	<b>% Bias</b>	<b>Confidence Interval around % Bias</b>
Acetaminophen	60 mg/dL	20 mg/dL					
	120 mg/dL	20 mg/dL					
	250 mg/dL	20 mg/dL					

688

689 In your 510(k) submission you should include a detailed description of the study design,  
690 all data collected in this study, the summary tables indicated above, and a description of  
691 the conclusions drawn from the study.

692

693

## 694 **2. Hematocrit**

695 *Study Design:*

696 Because a reasonably sized user evaluation study may not include the full range of  
697 hematocrit values expected in the intended use population, you should perform a separate  
698 study to determine how much analytical error is contributed by varying hematocrit levels.  
699 This should constitute a bench study designed to evaluate the effect of hematocrit on the  
700 performance of your SMBG to assess whether the potential for errors affects patient  
701 safety in the intended use population across your claimed hematocrit range. The observed  
702 hematocrit levels may be very broad in the intended use population for this type of  
703 device; the majority of intended users may reasonably be expected to have hematocrit  
704 levels between 20% and 60%. Therefore, we recommend 20-60% as the claimed  
705 hematocrit range for this type of device. If your device is subject to significant

### *Contains Nonbinding Recommendations*

706 interference from hematocrit within that range, you should include limitation statements  
707 in your labeling cautioning against use when certain physiological conditions are present  
708 or suspected (e.g., anemia, etc.). Because lay-users generally have no way to adequately  
709 determine their hematocrit status, SMBGs should be able to adequately measure glucose  
710 across the range of 30-55% hematocrit (which includes the greatest proportion of users).  
711 If your SMBG cannot detect glucose across this range, it is possible that your device may  
712 present new technological characteristics from the predicate that raise different questions  
713 of safety and effectiveness and may not be determined to be substantially equivalent.

714  
715 You should evaluate hematocrit interference by measuring blood samples containing  
716 various glucose concentrations. The samples should be prepared to contain designated  
717 levels of hematocrit that span the claimed hematocrit range for the device. Blood samples  
718 may be altered by spiking or allowing them to glycolyze to obtain desired glucose  
719 concentrations. Specific percentages of hematocrit may be achieved for each sample by  
720 manipulating the plasma to packed cell ratio following centrifugation. Hematocrit levels  
721 tested should span the claimed range in 5% intervals. Testing across the hematocrit range  
722 in 5% intervals allows for a more accurate assessment of bias from hematocrit  
723 interference than using broader intervals. For example, if your claimed hematocrit range  
724 is from 20-60%, you should test samples at 20, 25, 30, 35, 40, 45, 50, 55, and 60%  
725 hematocrit. The samples should also span the claimed measuring range for blood  
726 glucose. Samples should include 5 different blood glucose concentrations evenly spread  
727 and targeted to the following ranges: 30 – 50, 51 – 110, 111 – 150, 151 – 250, and 251 –  
728 400 mg/dL.

729  
730 Each sample should be tested on the comparator method in multiple replicates (e.g., we  
731 recommend a minimum of 4 replicates). A mean of the comparator measurements should  
732 give greater confidence in the true glucose concentration of the sample.

733  
734 You should test a minimum of 3 test strip lots to evaluate interference from hematocrit.  
735 Each sample should be tested on your new SMBG in replicates of 30 (10 replicates per lot  
736 of test strips, for a total of 30 replicates per sample). Each replicate should be compared  
737 to the average comparator value for the sample and a bias and % bias calculated. The  
738 percent bias for each replicate should be used to produce an average percent bias for the  
739 sample (with 95% confidence intervals).

740  
741 Because hematocrit interference is only one of the variables that can contribute to the  
742 overall analytical error of the system, it is important that it represent only a portion of the  
743 allowable error for the system. For this reason, bias observed in this study, for glucose  
744 concentrations greater than or equal to 75 mg/dL should be less than 8% on average, and  
745 no individual value should have a bias of greater than 15% relative to the comparator  
746 method. For samples less than 75 mg/dL glucose the absolute bias (mg/dL) should be  
747 reported (with 95% confidence intervals) and justified for clinical impact. For all results  
748 that are outside of the criteria described above, you should provide a clinical justification  
749 for the observed data and describe why the potential for that error due to hematocrit  
750 interference does not affect patient safety when extrapolated to the intended use setting.

*Contains Nonbinding Recommendations*

751

752 *Data Analysis:*

753 You should provide raw data sets as well as a summary of the hematocrit interference  
754 study (see recommended summary format in Table 5 and Table 6 below). Please note  
755 that the summary tables should be presented separately for each test strip lot and glucose  
756 level tested.

757

758 **Table 5: Sample summary format for hematocrit (Hct) results of samples with**  
759 **glucose concentrations <75 mg/dL:**

760 *Lot #, Glucose Level # (mg/dL)*

<b>Mean Glucose Value (Comparator)</b>	<b>Hct (%)</b>	<b>Mean Glucose Value (Meter)</b>	<b>Bias (mg/dL)</b>	<b>95% Confidence Intervals around Bias</b>	<b># of Measurements &gt; +/- 10 mg/dL</b>	<b>Clinical Justification</b>

761

762 **Table 6: Sample summary format for hematocrit (Hct) results of samples with**  
763 **glucose concentrations ≥75 mg/dL:**

764 *Lot #, Glucose Level # (mg/dL)*

<b>Mean Glucose Value (Comparator)</b>	<b>Hct (%)</b>	<b>Mean Glucose Value (Meter)</b>	<b>Bias (mg/dL)</b>	<b>% Bias</b>	<b># of Measurements &gt; +/- 15% Bias</b>

765

766 You should include in your 510(k) submission a detailed description of the study design, a  
767 list of all data collected in this study, the summary tables indicated above, and a summary of  
768 the conclusions drawn from the study.

769

770 **E. Flex Studies**

771 Compared to professional healthcare settings, there are typically fewer controls in place in  
772 home use settings to mitigate the risk of erroneous results. In addition, users are often  
773 untrained and may not know how to identify or address an erroneous result. It is therefore  
774 assumed that devices intended for home use by lay-users are designed so the risk of an  
775 erroneous result should be far less than with laboratory-based tests. You should therefore  
776 demonstrate that your SMBG design is robust (e.g., insensitive to environmental and  
777 usage variation) and that all known sources of error have been assessed through a detailed  
778 risk assessment and are effectively controlled. In general, flex studies should be used to  
779 demonstrate robust design while risk management should be used to demonstrate  
780 identification and effective control of error sources, although the two are not mutually  
781 exclusive.

782

783 Most risk control measures should be fail-safe mechanisms or failure alert mechanisms.  
784 Examples of fail-safe mechanisms are lock-out functions to ensure that a SMBG does not

### *Contains Nonbinding Recommendations*

785 provide a result when test conditions are inappropriate, such as when there is a  
786 component malfunction or operator error. Other examples are measures within the SMBG  
787 to prevent operator error, such as guides or channels that prevent improper strip  
788 placement. We recommend that the SMBG design incorporates fail-safe mechanisms  
789 whenever it is technically practicable. If fail-safe mechanisms are not technically  
790 practicable for some risks, failure alert mechanisms should be used. Failure alert  
791 mechanisms notify the operator of any SMBG malfunction or problem. These may  
792 include measures such as internal procedural controls or electronic controls. Devices with  
793 such mechanisms allow the operator to correct the error, or put the operator on notice that  
794 the results will be unreliable due to the error. For example, in cases where the result  
795 exceeds the reportable range (e.g., extremely high or low glucose result) and the result is  
796 a critical value, the device should give a message such as "high" or "low."

797  
798 Flex studies, or studies that stress the operational boundaries of a SMBG should be used  
799 to validate the insensitivity of the test system to performance variation under stress  
800 conditions. Where appropriate, flex studies should also be used to verify and/or validate  
801 the effectiveness of control measures at operational limits. Flex studies are particularly  
802 important for SMBGs as these devices are intended for use by lay-users and undergo a  
803 variety of environmental and user-associated conditions that could affect system  
804 performance.

805  
806 In order to identify all relevant flex studies for your SMBG, we recommend that you  
807 conduct a systematic and comprehensive risk analysis that identifies all potential sources  
808 of error, including test system failures and operator errors, and identify which of these  
809 errors can lead to a risk of a hazardous situation. You should then identify control  
810 measures, including fail-safe mechanisms and failure alert mechanisms that will reduce  
811 risks for these sources of error. When the control measures have been implemented, you  
812 should (1) verify that each control measure has been properly implemented, and (2) verify  
813 and/or validate the effectiveness of each control measure. When appropriate, flex studies  
814 should be used to verify and/or validate the effectiveness of these control measures.

815  
816 Below we have identified several flex studies that you should perform and include in the  
817 510(k) submission of your SMBG. At the same time, we encourage you to continue to  
818 perform risk analyses to determine whether your device includes any unique or new  
819 features that should be validated through additional flex studies.

820  
821 If your SMBG does not perform adequately in flex studies, we recommend you either  
822 provide a justification, determined by means of thorough risk analysis, as to why adequate  
823 performance in that flex study is not required for safe and effective use of the device, or  
824 indicate an additional validated control mechanism implemented.. FDA will review any  
825 justifications to determine whether the proposed risk mitigations are adequate to protect  
826 patients.

827  
828 In the case of the following flex studies, verification should include performance testing;  
829 however, it is acceptable for you to provide documentation indicating that flex studies



***Contains Nonbinding Recommendations***

830 have been conducted in accordance with an FDA-recognized industry standard in your  
831 510(k) submission. We recommend you include the type of testing performed, the  
832 reference standard followed, the acceptance criteria, and whether the SMBG passed  
833 testing requirements.

834

835 The flex studies we recommend performing in this manner are:

836

- 837 • Mechanical Vibration Testing
- 838 • Shock Testing
- 839 • Electromagnetic compatibility (EMC) Testing
- 840 • Electrostatic Discharge/Electromagnetic Interference Testing

841

842 Unless otherwise indicated, we recommend that you clearly identify all flex studies  
843 performed on your device in your 510(k) submission. A detailed description of the  
844 following attributes should be included in your 510(k) submission:

845

- 846 • Study goal
- 847 • Study protocols
- 848 • Methods used to apply samples to test strips
- 849 • Description of sample type and any anticoagulants used
- 850 • Study results
- 851 • Description of conclusions made from the study

852

853 We have also identified additional flex studies (described below) that we recommend be  
854 performed in order to demonstrate adequate system performance in intended use settings.  
855 A list of these recommended flex studies as well as recommended study designs are  
856 included below. These flex studies should be performed using fresh venous or capillary  
857 whole blood samples, not control solutions.

858

859 **1. Test Strip Stability Testing**

860 You should perform studies that assess test strip performance throughout the test strip  
861 stability claims, including closed and open vial claims. Three studies should be performed  
862 to support test strip stability: 1) closed vial stability (shelf life) should be performed to  
863 assess the recommended shelf life and conditions when the vial is stored closed  
864 throughout the claimed expiration dating, at different combinations of temperature and  
865 humidity spanning the recommended storage conditions; 2) open vial stability should be  
866 performed to mimic conditions under which an individual would actually use the strips  
867 where the vial is opened and closed throughout its claimed open vial life and stored at  
868 different combinations of temperature and humidity spanning the recommended storage  
869 conditions; and 3) extended open vial stability that mimics use of test strips from vials  
870 that have been left completely open for the duration of the claimed test strip open vial life  
871 when stored at different combinations of temperature and humidity spanning the  
872 recommended storage conditions. We suggest that you submit only the study protocols for

## *Contains Nonbinding Recommendations*

873 these test strip stability assessments, the acceptance criteria, and the conclusions of any  
874 studies which have been completed.

875

876 These studies (shelf life, open vial and extended open vial) should be designed to span  
877 both the claimed temperature range and humidity range at various time points throughout  
878 the duration of the respective claim. The time points that are assessed (e.g., 1 month, 3  
879 months, 2 years) should be specified in the protocol. Combinations of real-time and  
880 accelerated stability studies are acceptable. However, if accelerated studies are provided,  
881 real-time studies should be ongoing and the protocols and acceptance criteria should be  
882 provided for both study types.

883

884 You should perform adequate precision and accuracy evaluations at each identified time  
885 point. Examples of such studies are described below. Through these evaluations, you  
886 should demonstrate that the precision and accuracy calculated in these studies are within  
887 the labeled performance of the SMBG.

888

889 *Precision Evaluation:*

### Precision with Control Materials

891 This study should be completed over 5 days and use glucose controls. At least two  
892 meters should be included in this study and at least 10 measurements should be taken  
893 per glucose control level, per meter.

894

### Precision with Whole Blood Samples

896 This study should use whole blood samples spanning the claimed measuring range of  
897 the SMBG. Samples may be altered by spiking with glucose or allowing the samples  
898 to glycolyze in order to evaluate the extreme ends of the system's claimed measuring  
899 range. At least two meters should be included in this study and at least 10  
900 measurements should be taken per glucose level, per meter.

901

902 *Accuracy Evaluation:*

903 This study should be performed using whole blood samples that span the claimed  
904 measuring range of the SMBG. It is acceptable for samples to be spiked with a known  
905 concentration of glucose or allowed to glycolyze to achieve the desired concentration in  
906 order to evaluate the extreme ends of the system's measuring range. Glucose  
907 concentrations spanning the claimed measuring range (e.g., 30-50, 100-150, 200-300,  
908 350-500 mg/dL) should be measured with the SMBG and compared to values obtained  
909 with the comparator method.

910

## **2. System Operating Conditions Testing**

912 You should perform a study to assess the performance of your SMBG when used under  
913 various operating temperature and humidity conditions. These studies should be designed  
914 to represent actual use conditions experienced by SMBG users. Tested temperature and  
915 humidity ranges should not only cover the operating ranges that adequately reflect the  
916 intended use environment, and that are specified in the device labeling, but should also  
917 stress the SMBG by including ranges outside of the claimed operating range. Testing

## *Contains Nonbinding Recommendations*

918 should incorporate the four extreme temperature and humidity combinations (high  
919 temperature/low humidity, low temperature/high humidity, high temperature/high  
920 humidity, low temperature/low humidity). Measurements made on whole blood samples  
921 with your candidate device under various operating temperature and humidity conditions  
922 should be compared to values obtained with the comparator method.

923

924 Separate testing of test strip and meter shipping and storage conditions is not necessary if  
925 the temperature and humidity studies outlined here use only packaged blood glucose  
926 meters and blood glucose test strips that have undergone appropriate storage conditions  
927 and the longest possible shipping duration (both as specified by the manufacturer).

928

929 You should also include in your 510(k) submission a summary of any identified outliers  
930 that were excluded from statistical analysis, the method of outlier identification and the  
931 results of outlier investigations.

932

933 We also encourage manufacturers to consider ways in which temperature and/or humidity  
934 detectors might be incorporated into test strip containers to alert users when strips have  
935 not been handled correctly or stored according to recommended and validated conditions.

936

### **3. Altitude Effects**

937  
938 Relative to sea level, high altitude comprises a complex set of environmental differences  
939 and can induce multiple physiological changes, any or all of which might interfere with  
940 your SMBG's performance. For example, high altitude often involves extremes of  
941 temperature and humidity and can result in changes to hematocrit and blood pressure.  
942 The intended use environment of SMBGs in the United States includes high altitude  
943 conditions and therefore, manufacturers should conduct studies on the effects of altitude  
944 on their SMBG device or provide a justification for why altitude does not have an effect  
945 on the performance of their SMBG.

946

947 An altitude effects study should compare results from whole blood samples with your  
948 candidate device at the different high altitude conditions relative to the comparator  
949 method. These studies should also include a pressure change. Studies based on oxygen  
950 tension instead of pressure change are not adequate, because oxygen tension is only one  
951 component that changes with altitude. Altitude pressure changes can be accomplished by  
952 physically increasing altitude (e.g., in an airplane, on a mountain), or by simulating  
953 increasing altitudes and atmospheric conditions in a pressurized chamber. Results should  
954 support the altitude labeling claim for your device. You should provide your definition  
955 for terms, such as "sea level". The definition of sea level should not extend above 500  
956 feet. You should test your SMBG at a minimum of 10,000 feet above sea level.

957

958

959

960

### **4. Error Codes for Samples Outside the Measuring Range**

## *Contains Nonbinding Recommendations*

961 You should perform adequate analyses to demonstrate that your meter provides the  
962 appropriate error codes when measured glucose concentrations are outside of the  
963 SMBG's claimed measuring range, and include these results in your 510(k) submission.  
964

### **5. Short Sample Detection**

965 Blood glucose measurement from short samples (samples of reduced blood volume) can  
966 lead to inaccurate results. To avoid the risk of inaccurate results, SMBGs should be able  
967 to detect that a short blood sample has been applied to the test strip and should not  
968 provide a result to the user. Short sample detection systems should not rely on visual  
969 verification by the user.  
970

971  
972 The volume required to classify a test sample as a short sample is dependent upon the  
973 SMBG device. In your short sample detection studies you should include blood samples  
974 with known glucose concentrations in the following three ranges: 50-65 mg/dL, 100-120  
975 mg/dL, and 200-250 mg/dL. You should test blood samples with your candidate SMBG  
976 at each of the glucose concentrations listed above. Results obtained from the candidate  
977 device should be compared to the comparator method. Blood samples with serially  
978 reduced volumes should be measured on the device until an error is either generated by  
979 the device or the test result falls outside of the device's claimed performance  
980 characteristics. In your 510(k) submission you should describe the results from both the  
981 candidate device and the comparator method, as well as include the sample volumes  
982 tested for each glucose concentration range.  
983

### **6. Sample Perturbation Study**

984 Sample perturbation occurs when a user has applied an appropriate volume of blood to  
985 the test strip for glucose measurement but an event such as wicking of blood away from  
986 the test strip, flicking of the test strip or flicking of the meter occurs during the start of the  
987 measurement and alters the volume of the initial sample application. You should  
988 adequately demonstrate how your SMBG handles sample perturbation through a sample  
989 perturbation study.  
990

991  
992 In a sample perturbation study, a sample should be applied to the test strip and after the  
993 SMBG device has begun to read the sample, but before the measurement is complete, the  
994 test strip should be perturbed. The sample perturbation study should incorporate blood  
995 samples with known glucose concentrations in the following three ranges: 50-65 mg/dL,  
996 100-120 mg/dL, and 200-250 mg/dL. In your 510(k) submission you should describe  
997 your protocol, including your specific method of perturbing the test sample, as well as  
998 meter results compared to the comparator method.  
999

### **7. Intermittent Sampling**

1000 Intermittent sampling occurs when a short sample is applied to a test strip, a glucose  
1001 measurement begins, and the user adds more sample to the test strip before the glucose  
1002 measurement is complete. You should adequately demonstrate how your SMBG handles  
1003 intermittent sampling by conducting an intermittent sampling study.  
1004  
1005

## *Contains Nonbinding Recommendations*

1006 The intermittent sampling study should incorporate blood samples with known glucose  
1007 concentrations in the following three ranges: 50-65, 100-120, and 200-250 mg/dL. You  
1008 should perform intermittent sampling studies that are representative of actual events. For  
1009 instance, approximately one half of the sample should be applied to the test strip prior to  
1010 the start of sample measurement, then the other half of the sample should be applied to  
1011 the strip after a set period of time, such as once the sample starts reading. For systems  
1012 that allow a second sample of blood to be added to the test strip without producing an  
1013 error message, different time delays throughout the claimed period of second application  
1014 should be tested once the sample starts reading, but before the measurement is complete.  
1015 You should describe how the device responds to this scenario in your 510(k) submission,  
1016 including whether a result is reported, whether this result is accurate (relative to the  
1017 comparator method) and when an error code is reported.  
1018

### **8. Testing with Used Test Strips**

1019 You should perform a study to demonstrate how your SMBG device performs when a  
1020 used test strip is inserted. We recommend that SMBG devices be designed to  
1021 automatically recognize the insertion of used test strips. Insertion of used test strips into a  
1022 SMBG should not provide glucose measurement results to the user. If an automatic used  
1023 test strip recognition function has been incorporated into your SMBG, you should  
1024 perform a flex study to demonstrate the functionality of this recognition system. In your  
1025 510(k) submission you should provide the study protocol, acceptance criteria and results  
1026 of your used test strip study.  
1027  
1028

## ***F. Meter Calibration and Quality Control Materials***

1029 The use of external control solutions allow users to periodically check that the SMBG and  
1030 test strips are working together properly and that the device is performing correctly. In  
1031 order to further promote the use of external control solutions by the user, at least one level  
1032 of control material should be included along with each test strip vial, and at least one  
1033 additional level of control material should be specified in the labeling as available to the  
1034 user. We recommend you review FDA’s guidance entitled “Guidance for Industry and  
1035 FDA Staff - Assayed and Unassayed Quality Control Material”  
1036 ([http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocument](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm079179.htm)  
1037 [s/ucm079179.htm](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm079179.htm)) and submit the recommended information to support clearance of your  
1038 assayed glucose quality control material.  
1039

1040  
1041 Control solutions provided should not be labeled in a descriptive manner such as “low,”  
1042 “normal,” or “high” since that may be misleading to the user; users may confuse a label  
1043 that says “normal” as meaning that value is a clinically normal value even when the  
1044 control concentration is not within the normal range that is recommended by that  
1045 individual user’s physician. Therefore, control solutions should be labeled non-  
1046 descriptively (e.g., numerically- 1, 2, 3).  
1047

1048 For a description of more points to consider regarding quality control materials, please  
1049 reference FDA’s guidance entitled “In Vitro Diagnostic Devices: Guidance for the

## *Contains Nonbinding Recommendations*

1050 Preparation of 510(k) Submissions – Appendix K – Points to Consider for Review of  
1051 Calibration and Quality Control Labeling for In Vitro Diagnostic Devices”  
1052 (<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM094139.pdf>).  
1053  
1054

1055 You should describe in your 510(k) submission how the candidate device recognizes and  
1056 distinguishes control materials from patient specimens, either automatically or manually  
1057 by the user, as well as explain how the system compensates for differences between test  
1058 strip lots (i.e. how the meter is calibrated or coded for each test strip lot).  
1059

## 1060 **VII. Test Strip Lot Release Criteria**

1061  
1062 Your test strip lot release criteria should be set to ensure consistent performance of your  
1063 SMBG test strips. You should provide a description of the lot release criteria and a summary  
1064 of the sampling scheme in your 510(k) submission. In addition, you should explain how the  
1065 system compensates for differences between strip lots or strip types.  
1066

1067 We recommend that you select a sampling scheme appropriate for the operation of your  
1068 SMBG device and test each outgoing test strip lot or batch using the precision and accuracy  
1069 evaluations described below. Your test strip lot release criteria should be designed to ensure  
1070 that all released lots conform to the labeled SMBG performance *in the hands of the intended*  
1071 *user*. Therefore, these criteria should be more stringent than the criteria used to evaluate total  
1072 error in the performance studies. Estimates of the SMBG’s imprecision and average bias  
1073 may be used to determine appropriate criteria. Examples of such testing are described below.  
1074

### 1075 *Precision Evaluation:*

#### 1076 Precision using Control Materials

1077 This study should be completed over 5 days and use glucose controls. At least two  
1078 meters should be included in this study and at least 10 measurements should be taken  
1079 per control, level per meter.  
1080

#### 1081 Precision using Whole Blood Samples

1082 This study should include at least 10 measurements using whole blood samples  
1083 spanning the claimed measuring range of the SMBG. Spiking samples with glucose  
1084 or including samples in which glucose was allowed to glycolyze is acceptable in  
1085 order to evaluate the extreme end of the system’s measuring range. At least two  
1086 meters should be included in this study and at least 10 measurements should be  
1087 taken per glucose level, per meter.  
1088

### 1089 *Accuracy Evaluation:*

1090 The accuracy evaluation should be performed using whole blood samples that span the  
1091 claimed measuring range of the SMBG. It is acceptable for samples to be spiked with a  
1092 known concentration of glucose, or to include samples in which the glucose was allowed to  
1093 glycolyze in order to evaluate the extreme ends of the system’s measuring range. Glucose

*Contains Nonbinding Recommendations*

1094 concentrations should be measured using the SMBG and compared to the comparator  
1095 method.  
1096

1097 **VIII. Third Party Test Strips**

1098  
1099 Third party test strips refer to test strips manufactured and distributed by a company other  
1100 than the company that manufactures and distributes the glucose meter. Third party test strip  
1101 manufacturers should ensure that they are aware of any design changes to the meter because  
1102 such changes could affect compatibility of the test strip with the meter. Because test strips  
1103 and meters work as integral systems, third party test strip manufacturers should sufficiently  
1104 address in their 510(k) submissions how they will mitigate the risk of incorrect results due to  
1105 meter design changes. One way to effectively ensure that the third party test strip  
1106 manufacturer is made aware of any design changes to the meter is by having in place an  
1107 agreement between the third party test strip manufacturer and the meter manufacturer.  
1108

1109 **IX. Software**

1110  
1111 For software descriptions of SMBGs, their components, and accessories, we recommend that  
1112 you review FDA’s guidance entitled “Guidance for the Content of Premarket Submissions for  
1113 Software Contained in Medical Devices”  
1114 (<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089593.pdf>). Generally, FDA considers blood glucose meters to be moderate  
1115 level of concern devices because glucose results will be the basis for treatment, including  
1116 determination of insulin dosage by the patient or health care provider. Incorrect glucose  
1117 results or failure of the software to detect an error could result in improper diabetes  
1118 management. Also see Section V above regarding software descriptions in your 510(k)  
1119 submission.  
1120  
1121

1122 **X. Labeling**

1123  
1124 The labeling of a SMBG includes the user manual, the quick start guide (optional), the  
1125 package inserts for both test strips and controls, and the box and container labels for the  
1126 meter, test strips, and control materials. The package inserts for test strips and controls, and  
1127 the user manual should be simple, concise, and easy to understand. Graphics such as line  
1128 drawings, illustrations, icons, photographs, tables, and graphs are very useful tools.  
1129 Manufacturers should ensure that the same terms are used consistently throughout the  
1130 labeling to identify the device and its parts, avoiding synonyms or alternate phrases. Symbols  
1131 should not be used in the labeling of devices intended for home use by the lay-user. We  
1132 recommend that you refer to the following documents for information on important principles  
1133 for developing clear and complete home use IVD labeling:  
1134

*Contains Nonbinding Recommendations*

- 1135 • FDA’s guidance entitled “Guidance on Medical Device Patient Labeling; Final  
1136 Guidance for Industry and FDA”  
1137 ([http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocu](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070782.htm)  
1138 [ments/ucm070782.htm](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070782.htm)).
- 1139 • CLSI GP-14: *Labeling of Home-Use In Vitro Testing Products; Approved Guideline*.
- 1140 • FDA’s Device Advice website entitled In Vitro Diagnostic Labeling Requirements  
1141 ([http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/Devi](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/DeviceLabeling/InVitroDiagnosticDeviceLabelingRequirements/default.htm)  
1142 [ceLabeling/InVitroDiagnosticDeviceLabelingRequirements/default.htm](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/DeviceLabeling/InVitroDiagnosticDeviceLabelingRequirements/default.htm)).

1143

1144 Technical information required by 21 CFR 809.10(b) should be described so that lay-users  
1145 can understand the information or locate the information, if necessary. Detailed technical  
1146 information (e.g., chemical details of test principle or statistical analyses of data) may be  
1147 presented in a separate section followed by clarifying statements appropriate for lay-users.

1148

1149 The 510(k) submission must include labeling in sufficient detail to satisfy the requirements of  
1150 21 CFR 807.87(e). Final labeling must also satisfy the requirements of 21 CFR 809.10.

1151

1152 The following items are intended to further assist sponsors in complying with the  
1153 requirements of 21 CFR 809.10 for test strip and meter labeling.

1154

- 1155 1. All device labeling must contain the proprietary and common names of the device. 21  
1156 CFR 809.10(a)(1) and 21 CFR 809.10(b)(1). The various test system components  
1157 should be named in such a way that they are recognized as belonging to the same  
1158 system or family of products (ABC blood glucose test system, ABC blood glucose  
1159 meter, ABC blood glucose test strips, etc.) to aid in identification of system  
1160 components.
- 1161 2. You must include the intended use of the product in your label and labeling  
1162 documents. 21 CFR 809.10(a)(2) and 21 CFR 809.10(b)(2). The intended use for  
1163 SMBGs for home use by lay-users should be similar to the example below:  
1164
- 1165 3. The XYZ Blood Glucose Monitoring System is intended for use in the quantitative  
1166 measurement of glucose in capillary whole blood from the finger. It is intended for  
1167 use by people with diabetes mellitus at home as an aid in monitoring the effectiveness  
1168 of a diabetes control program. The XYZ Blood Glucose Monitoring System is  
1169 intended to be used by a single person and should not be shared.  
1170
- 1171 4. The label and labeling must include warnings appropriate to the hazard presented by  
1172 the product. (21 CFR 809.10(a)(4) and 21 CFR 809.10(b)(5)(ii)).  
1173
- 1174 5. You should include the following warning *prominently* on the outer box label and  
1175 package insert.  
1176

1176

1177 **This device is not intended for use in healthcare or assisted-use settings such as**  
1178 **hospitals, physician offices, or long-term care facilities because it has not been**



*Contains Nonbinding Recommendations*

1179 cleared by FDA for use in these settings, including for routine assisted testing or as  
1180 part of glycemic control procedures.

1181  
1182 **Use of this device on multiple patients may lead to transmission of Human**  
1183 **Immunodeficiency Virus (HIV), Hepatitis C Virus (HCV), Hepatitis B Virus (HBV),**  
1184 **or other bloodborne pathogens.**

- 1185  
1186 1. The labeling must include the chemical, physical, physiological, or biological  
1187 principles of the procedure as per 21 CFR 809.10(b)(4). The discussion of these  
1188 principles should include identification and source of the enzyme and description of  
1189 the reaction. Labeling should specify whether results are determined in terms of  
1190 whole blood or plasma equivalents. SMBGs intended for use in the U.S. should  
1191 report results in terms of plasma equivalents.  
1192  
1193 2. The label must include a means by which the user may be assured that reagents meet  
1194 appropriate standards of identity, strength, quality and purity at the time of use as  
1195 described in 809.10(a)(6) and 21 CFR 809.10(a)(10).  
1196  
1197 3. The labeling must provide instructions for specimen collection and preparation. (21  
1198 CFR 809.10(b)(7)). Instructions should include a statement to users on the  
1199 importance of thoroughly washing with soap and water and drying the skin before  
1200 taking a sample, because contaminants on the skin may affect results. See also  
1201 instructions for cleaning and disinfection below.  
1202  
1203 4. The labeling must provide a step-by-step outline of recommended procedures (21  
1204 CFR 809.10(b)(8)), and operating instructions for the instrument (21 CFR  
1205 809.10(b)(6)(v)). Numbering, rather than bullets, should be used for clarity when  
1206 appropriate (e.g., procedural steps, etc.).  
1207  
1208 5. The labeling must include a statement of limitations of the procedure including  
1209 known extrinsic factors or interfering substances affecting results (21 CFR  
1210 809.10(b)(10)). You should include testing conditions that may cause clinically  
1211 significant errors (due to bias or imprecision) with your SMBG (e.g., specific drugs,  
1212 oxygen therapy, high altitude). You should indicate the most extreme conditions (e.g.,  
1213 the highest altitude, highest and lowest temperatures, etc.) at which the device has  
1214 been validated based on the results of performance testing.  
1215  
1216 6. The labeling should clearly indicate to users what display they can expect to see when  
1217 their measured glucose is lower or higher than the claimed measuring range of the  
1218 meter. For example, meter XYZ has a measuring range that goes down to 50 mg/dL.  
1219 All glucose values measured below 50 mg/dL will provide an appropriate message  
1220 indicating the results are below the meter range. Meter XYZ's labeling would include  
1221 a statement explaining this error code: "When your glucose value is less than 50  
1222 mg/dL you will see the following error code 'Less than 50'."  
1223

### *Contains Nonbinding Recommendations*

- 1224 7. The labeling must describe details of calibration and of quality control procedures and  
1225 materials (21 CFR 809.10(b)(8)(v) and 21 CFR 809.10(b)(8)(vi)). This is to help  
1226 ensure optimal performance of the SMBG. This section should include  
1227 recommendations for how and when to perform quality control checks and  
1228 instructions for what to do if the control material values are not within the  
1229 manufacturer's allowable range. As part of the quality control information in your  
1230 labeling, we recommend sponsors advise users that they should periodically review  
1231 their technique and compare a result obtained with their meter to a result obtained  
1232 using a laboratory method or a well-maintained and monitored system used by their  
1233 healthcare provider.  
1234
- 1235 8. The labeling must include expected values (21 CFR 809.10(b)(11)). FDA  
1236 recommends that the expected values should be those for non-diabetics. FDA does  
1237 not recommend including additional ranges adjusted for diabetics because such ranges  
1238 are individualized and determined by the clinician. The expected values should be  
1239 cited from in-house studies or up-to-date reference sources.  
1240
- 1241 9. The labeling must include specific performance characteristics (21 CFR  
1242 809.10(b)(12)). Sponsors should briefly describe all studies and summarize results in  
1243 the package inserts. FDA recommends that this include performance data summaries  
1244 from in-house and user studies. For presentation of accuracy in particular, see the  
1245 charts below for an example. Performance should be presented separately for each  
1246 anatomical site and matrix.  
1247
- 1248 10. So that lay users have the ability to choose the SMBG that is right for them, it is  
1249 important to clearly describe the accuracy of the device in a way that is easy for them  
1250 to understand. It is also important for this information to be located in a prominent  
1251 place in product labeling so that lay-users can understand the performance of an  
1252 individual SMBG both prior to purchase and also when they are learning to use the  
1253 device they have purchased. Therefore, the outer box labeling, the package insert for  
1254 the test strip, and the user manual should all have easy to understand depictions of the  
1255 clinical study results.  
1256
- 1257 11. In the package insert for the test strips and the user manual for the SMBG,  
1258 accuracy information should be placed prominently within the labeling. We  
1259 recommend that this information be included in the section where the labeling  
1260 describes how a user will obtain a result. In the test strip package insert, this section  
1261 should be large and centrally placed so that users understand the performance of the  
1262 system using these test strips. We recommend the following types of presentations to  
1263 convey the results of your accuracy studies in the device user manual and test strip  
1264 package inserts.  
1265

*Contains Nonbinding Recommendations*

**Suggested Representation of Accuracy for Home Use by Lay-Users - Example**

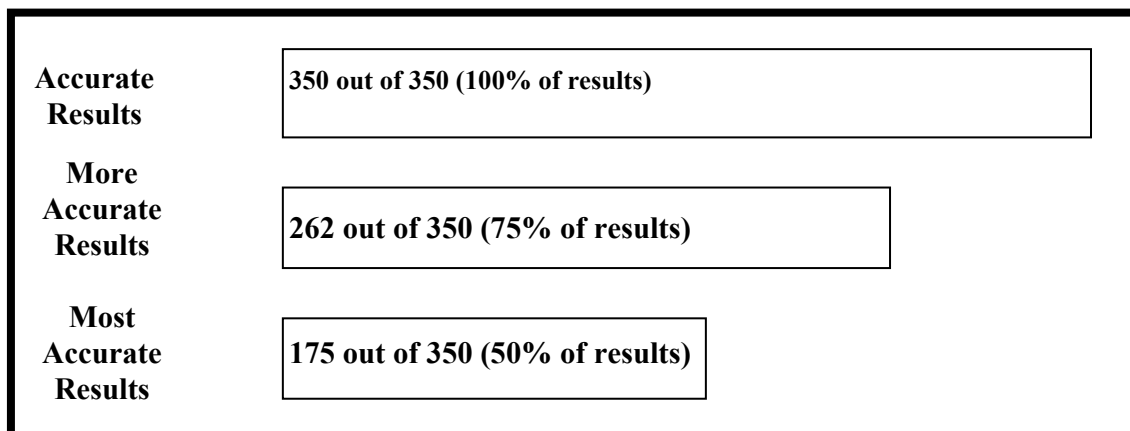
Your ABC Meter result may vary slightly from your actual blood glucose value. This may be due to slight differences in technique and the natural variation in the test technology.

The chart below shows the results of a study where 350 typical users used the ABC meter to test their blood glucose level. For example, in this study, the ABC meter gave results within 15% of their true blood glucose level 340 out of 350 times.

<b>Difference range between the true blood glucose level and the ABC meter result.</b>	<b>Within 5 %</b>	<b>Within 10 %</b>	<b>Within 15 %</b>	<b>Within 20%</b>
The percent (and number) of meter results that match true blood glucose level within x%	57% (200/350)	94% (330/350)	97% (340/350)	100% (350/350)

1266  
1267  
1268  
1269  
1270  
1271  
1272

Accuracy information should also be included on the SMBG outer box and test strip outer box labeling as well as in the test strip package inserts and user manual. We recommend that this outer box label accuracy information refer readers to the package insert and graphically represent the user study data. An example of this type of presentation is shown below. Numbers represent the number of meter results that were within the level of accuracy shown, relative to the laboratory device.



1273  
1274  
1275  
1276  
1277

<b>Accuracy key</b>	<b>Percentages listed are meter result as compared to laboratory result</b>
Accurate Results	Meter result is +/-15% of laboratory result
More Accurate Results	Meter result is +/-10% of laboratory result
Most Accurate Results	Meter result is +/-5% of laboratory result

1278  
1279

### *Contains Nonbinding Recommendations*

- 1280 1. The labeling must describe the principles of operation for the instrument as well as  
1281 service and maintenance information (21 CFR 809.10(b)(6)). Labeling should include a  
1282 list or summary of error messages, descriptions of what those error messages mean, and  
1283 appropriate troubleshooting procedures for those error messages.  
1284
- 1285 2. You should provide in the labeling a working U.S. toll free telephone number for user  
1286 assistance in the labeling, and include hours of operation and U.S. time zone, if  
1287 applicable. If user assistance is not provided 24 hours/7 days a week/365 days a year,  
1288 sponsors should provide instructions for what measures the user should take when user  
1289 assistance is not available.  
1290
- 1291 3. The label and labeling must include statements of warning or precautions as appropriate  
1292 to the hazard presented by the product (21 CFR 809.10(a)(4) and 21 CFR  
1293 809.10(b)(5)(ii)). We recommend that you include instructions to lay-users to contact  
1294 their healthcare provider if they obtain results that are not consistent with the way they  
1295 feel, and to not change their medication regimen without approval from a healthcare  
1296 provider.  
1297

1298 You should clearly and prominently state the important warnings for this device towards  
1299 the beginning of the labeling, in a section containing **Important Safety Instructions**.  
1300 Important warnings and safety information should be included on all test system  
1301 instructions (User manual, test strip labeling, etc.).  
1302

1303 You should stress the risk of disease transmission when using SMBGs and reference any  
1304 relevant public health notifications, standard practice guidelines, or other resources  
1305 available to users. At a minimum, the following warnings should be included:  
1306

- 1307 • The meter and lancing device are for single patient use. Do not share them with  
1308 anyone including other family members! Do not use on multiple patients!
- 1309 • All parts of the kit are considered biohazardous and can potentially transmit  
1310 infectious diseases, even after you have performed cleaning and disinfection.

1311

1312 You should include these references:

1313

- 1314 • *“FDA Public Health Notification: Use of Fingerstick Devices on More than One  
1315 Person Poses Risk for Transmitting Bloodborne Pathogens: Initial Communication”  
1316 (2010) <http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm224025.htm>*
- 1317
- 1318 • CDC website on *“Infection Prevention during Blood Glucose Monitoring and Insulin  
1319 Administration” <http://www.cdc.gov/injectionsafety/blood-glucose-monitoring.html>*  
1320

1321

1322 In the section(s) describing **how to obtain a blood sample**, you should reiterate the risk  
1323 of bloodborne pathogen transmission. You should stress that a lancing device is intended  
only for a single user and should not be shared. You should stress that users should clean

## *Contains Nonbinding Recommendations*

1324 their hands thoroughly with soap and water after handling the meter, lancing device, or  
1325 test strips.

1326

1327 The user manual should contain detailed instructions for how and when users should  
1328 perform **cleaning and disinfection procedures** for the meter based on the validation  
1329 studies performed. Specifically the instructions should include the following:

1330

- 1331 • An explanation of why the cleaning and disinfection should be performed in language  
1332 that is appropriate for the intended user. You should explain the difference between  
1333 “cleaning” and “disinfection.”
- 1334 • The recommended frequency a user should clean and disinfect the device. For  
1335 example, the meter should be cleaned and disinfected at a minimum of once per week.  
1336 An explanation should be provided for how this number relates to the number of  
1337 validated cycles over the life of the device. The use life of the device should be  
1338 clearly stated.
- 1339 • A list of the materials needed for cleaning and disinfection should be provided.  
1340 Instructions on how these products can be purchased or prepared need to be clearly  
1341 outlined.
- 1342 • A detailed procedure describing what parts of the device should be cleaned and  
1343 disinfected, the amount of time the cleaner or disinfectant needs to remain on the  
1344 meter (contact time), etc. You should include graphics/photographs to assist the user.
- 1345 • A statement that users should clean hands thoroughly with soap and water after  
1346 handling the meter, lancing device, or test strips.
- 1347 • A contact telephone number for technical assistance or questions should be  
1348 prominently listed in the cleaning and disinfection section along with a list of signs of  
1349 external deterioration and deteriorating performance that the user should look for.

1350

1351 4. If studies have not been presented supporting the use of alternative site testing (AST) for  
1352 a SMBG, you should include a prominent warning in the package insert and user manual  
1353 against use of the device for AST. Sampling from anatomical sites other than the  
1354 fingertip, i.e., forearm, upper arm, thigh, calf, palm, may be indicated for some SMBGs.

1355

1356 Some users may prefer obtaining blood from alternative sampling sites because of less  
1357 pain or greater choice in puncture sites. However, studies have shown that during times  
1358 of rapidly changing glucose (i.e., after meals, medication, or exercise), the glucose level  
1359 in blood from the alternative site may be significantly different from the glucose level in  
1360 blood from the fingertip. Additionally, glucose levels may not rise as high or fall as low  
1361 as levels in the fingertip. This can result in a delay, or a failure to detect, hypoglycemia  
1362 when glucose is measured in alternative sites during non-fasting times.

1363

1364 When alternative sampling sites have been validated, and are indicated, you should clarify  
1365 that results from these sites may lag behind fingertip samples during periods of glucose  
1366 change, or reduced peripheral circulation (e.g., shock).

1367

### *Contains Nonbinding Recommendations*

1368 You should include the following limitations relating to AST testing in your package  
1369 inserts:

1370

1371 • Alternative site sample results may be different from fingertip sample results when  
1372 glucose levels are changing rapidly (e.g., after a meal, after taking insulin, or during  
1373 or after exercise).

1374 • Do not rely on test results at an alternative sampling site, but use samples taken from  
1375 the fingertip, if any of the following applies:

- 1376 ○ you think your blood sugar is low.
- 1377 ○ you are not aware of symptoms when you become hypoglycemic.
- 1378 ○ the results do not agree with the way you feel.
- 1379 ○ after a meal.
- 1380 ○ after exercise.
- 1381 ○ during illness.
- 1382 ○ during times of stress.

1383 • Do not use results from alternative site samples to calibrate continuous glucose  
1384 monitoring systems (CGMS), or for insulin dose calculations.

1385

## Appendix 1. Sources of error to consider for SMBGs

1386  
1387  
1388  
1389  
1390  
1391  
1392  
1393  
1394  
1395

Table 7 below lists sources of error associated with the design, production, and use of SMBGs. We do not intend for this to be a complete list. You should consider all sources of error based on your knowledge of your specific device. Documents such as CLSI EP-18A and ISO 14971 also provide lists of preanalytical, analytical, and post-analytical errors to consider.

**Table 7 – Examples of Sources of Error**

Category	Source of error or failure
Operator	<p><b>Failure to follow procedure correctly, for example:</b></p> <ul style="list-style-type: none"> <li>• <b>Sample contamination</b></li> <li>• <b>Incorrect specimen collection (e.g., poor lancing technique and incorrect volume)</b></li> <li>• <b>Application of an insufficient amount of blood to the strip or incorrect application of blood to strip</b></li> <li>• <b>Use of a sample from an alternative site at inappropriate times or from a site not validated by the manufacturer</b></li> <li>• <b>Application of the specimen to the strip more than once (for example, if the user believes not enough specimen was added the first time)</b></li> <li>• <b>Incorrect insertion of strip into meter</b></li> <li>• <b>Inaccurate timing</b></li> <li>• <b>Use of contaminated, outdated, or damaged strips or reagents, including calibrators or quality control materials</b></li> <li>• <b>Failure to understand or respond to meter output.</b></li> <li>• <b>Errors in meter maintenance or cleaning</b></li> <li>• <b>Errors in calibration or failure to calibrate or otherwise adjust the meter or check performance with quality control materials, as directed by labeling</b></li> <li>• <b>Incorrect saving or use of stored data</b></li> <li>• <b>Improper storage or handling of the meter, calibrators, quality control materials or test strips, or maintenance of the meter</b></li> <li>• <b>Inadvertent changes of parameters (such as units of measurement)</b></li> <li>• <b>Failure to contact physician when necessary</b></li> <li>• <b>Use of strips not validated for use on the meter</b></li> </ul>
Reagent	<ul style="list-style-type: none"> <li>• <b>Expired strips or reagents</b></li> <li>• <b>Damaged or contaminated strips</b></li> <li>• <b>Failure of strips, calibrators, or quality control materials to perform adequately</b></li> </ul>

*Contains Nonbinding Recommendations*

	<ul style="list-style-type: none"> <li>• <b>Incorrect manufacturing; product fails to conform with specifications</b></li> <li>• <b>Incorrect dimensions of reagent strip</b></li> <li>• <b>Interference with chemical reaction on strip (e.g., reducing substances)</b></li> <li>• <b>Inadequate design of container for strips or other reagents; failure to prevent deterioration; failure of desiccant used to keep strips dry</b></li> </ul>
Environmental	<ul style="list-style-type: none"> <li>• <b>DEVICE EFFECTS</b> <ul style="list-style-type: none"> <li>• <b>Temperature</b></li> <li>• <b>Humidity</b></li> <li>• <b>Altitude; hyperbaric oxygen therapy conditions</b></li> <li>• <b>Electromagnetic radiation</b></li> <li>• <b>Visible light; sunlight</b></li> </ul> </li> <li>• <b>HUMAN FACTORS</b> <ul style="list-style-type: none"> <li>• <b>Lighting, glare off meter surfaces</b></li> <li>• <b>Distractions, visual and auditory</b></li> <li>• <b>Stressful conditions</b></li> <li>• <b>Limited manual dexterity</b></li> </ul> </li> </ul>
Software	<ul style="list-style-type: none"> <li>• <b>Confusing or obscure user prompts and feedback</b></li> <li>• <b>Incorrect mathematical algorithm</b></li> <li>• <b>Undetected or unrecognized signal errors</b></li> <li>• <b>Timing failure</b></li> <li>• <b>Incorrect storage of test results in memory, including matching result with correct patient or time of test</b></li> <li>• <b>Other software failures</b></li> </ul>
Hardware	<ul style="list-style-type: none"> <li>• <b>Electronic failure</b></li> <li>• <b>Physical trauma or vibration</b></li> <li>• <b>Damage to the device from incorrect strip dimensional tolerances (third party manufacturer)</b></li> <li>• <b>Electrostatic discharge</b></li> <li>• <b>Electromagnetic/radiofrequency interference</b></li> <li>• <b>Battery reliability, lifetime, and replacement</b></li> <li>• <b>Component(s) failure</b></li> <li>• <b>Incorrectly manufactured</b></li> </ul>



*Contains Nonbinding Recommendations*

System	<ul style="list-style-type: none"><li>• <b>Physical trauma or vibration</b></li><li>• <b>Incorrect calibration/adjustment (between lots of strips)</b></li><li>• <b>Calibration failure, interference, instability or use beyond the recommended period of stability.</b></li><li>• <b>Labeling not geared to intended user.</b></li><li>• <b>Meter or operation complexity not geared to intended user</b></li><li>• <b>Inadequate training</b></li></ul>
Clinical	<ul style="list-style-type: none"><li>• <b>Interference from endogenous substances.</b></li><li>• <b>Severe conditions (e.g., dehydration, hypoxia, hyperglycemic-hyperosmolar state, hypotension or shock, ketoacidosis).</b></li><li>• <b>Interference from other exogenous substances (e.g., maltose intravenous solutions)</b></li></ul>

1396

1397

## Appendix 2. Special 510(k)s and SMBGs

### What is a special 510(k) and how does it apply to your blood glucose meter submission?

A special 510(k) submission is an alternative to the traditional method of demonstrating substantial equivalence for certain modifications of a manufacturer's own previously cleared device that do not affect the intended use or alter the fundamental scientific technology. For such modifications, the Agency believes that the rigorous design control procedure requirements outlined in the Quality System Regulation (QS reg) [See 21 CFR part 820] produce highly reliable results that can form, in addition to the other 510(k) content requirements, a basis for the substantial equivalence determination.

As such, under the special 510(k) option, a manufacturer who is intending to modify his/her own legally marketed device will conduct the risk analysis and the necessary verification and validation activities to demonstrate that the design outputs of the modified device meet the design input requirements. Once the manufacturer has ensured the satisfactory completion of this process, a "Special 510(k): Device Modification" may be submitted.

### Eligibility for a Special 510(k)

To determine whether a modified SMBG is eligible to be submitted as a special 510(k), you should consult the FDA guidance entitled "The New 510(k) Paradigm - Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications - Final Guidance" ([www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080187.htm](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080187.htm)). Sponsors should also consult the information on FDA's website entitled "How to Prepare a Special 510(k)" (<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm134573.htm>).

As noted above, a special 510(k) is appropriate where the candidate device is a modification of a sponsor's own legally marketed device, which would serve as the predicate for the modified device. This usually means that the candidate device and predicate device are part of the same device design file. The existence of *similarities* between the predicate device A and candidate device B does not by itself necessarily mean that device B is a modification of device A.

FDA believes that to ensure the success of the special 510(k) option, there should be a common understanding of the types of device modifications that may gain marketing clearance by this path. As such, it is critical that Industry and Agency staff can easily determine whether a modification is appropriate for submission as a Special 510(k). To optimize the chance that a special 510(k) will be accepted for review, sponsors should evaluate each modification to ensure that the device modification does not: (1) affect the intended use or (2) alter the fundamental scientific technology of the device.

*Contains Nonbinding Recommendations*

1439 Based on FDA’s experience with blood glucose meters, we can offer the following list of  
1440 modifications that may or may not be eligible for review as a special 510(k). This list is not  
1441 intended to be all-inclusive.

1442

1443 **Modifications that are generally eligible for a Special 510(k):**

1444

- 1445 • Minor changes in user interface
- 1446 • Change in memory capabilities (e.g., adding the ability to store additional results)
- 1447 • Elimination of strip coding requirements through a restriction of test strip lot release  
1448 criteria
- 1449 • Addition of a voice (speaking) feature if the device is not intended for visually  
1450 impaired users

1451

1452 **Modifications that are generally NOT eligible for a Special 510(k):**

1453

- 1454 • Significant change in the sample volume applied to the glucose test strip
- 1455 • Addition of alternative sampling sites (e.g., adding the palm in addition to the  
1456 fingertip)
- 1457 • Addition of sample matrices (e.g., adding venous whole blood in addition to capillary  
1458 blood)
- 1459 • Change to the measuring algorithm used to calculate a glucose concentration
- 1460 • Change in enzyme used in the chemical reaction (e.g. from glucose dehydrogenase to  
1461 glucose oxidase)
- 1462 • Use of a test strip cleared for meter A for use on separately cleared meter B
- 1463 • Any modification that affects the intended use of the device
- 1464 • Any change in fundamental scientific technology

1465

1466 We recommend that you contact the Office of In Vitro Diagnostic Devices and Radiological  
1467 Health (OIR) to discuss any specific questions you have regarding your SMBG’s eligibility to  
1468 be submitted as a special 510(k).

1469