**Worksheet for**

**Developing a Plan for Actors to Test Conformance with the Profile Claim**

 A final step in testing conformance is the evaluation of the actor’s ability to achieve the performance stated in the claim. A plan for testing conformance with the claim can be developed using the following steps [1]:

**Table 1: Steps to Testing Compliance with Claim**

|  |  |  |  |
| --- | --- | --- | --- |
| **Step #** | **Description** | **CT Volumetry Example** | **Amyloid** |
| ***Test Precision*** |
| 1 | Identify test data for evaluating actor’s precision. Another option is to require the actor to generate test data. | A previously published test-retest dataset from Sloan Kettering will be used.  |  |
| 2 | Specify minimum # of subjects needed to evaluate precision. See Table 2 below for guidance. | The Sloan Kettering dataset has N=31 cases with test-retest data. In the CT Volumetry profile, a RC of 21% is claimed. From Table 2, if an actor has a RC of 15% or less, then with N=31, the actor has about 80% power to show that its RC is sufficiently low to be compliant. |  |
| 3 | State the methods for estimating actor’s precision  | For each case calculate the QIB measurement at time point 1 (denoted Yi1) and at time point 2 (Yi2) where *i* denotes the *i*-th case. For each case calculate: . Calculate: . Estimate the Repeatability Coefficient: .  | *Use the same boilerplate language* |
| 4  | Specify the statistical test to be used to assess conformance to the claim – **compliance endpoint (1)** | Let the RC in the claim statement be denoted δ (for CT Volumetry claim, δ=21%). Let θ denote the actor’s unknown precision. Test the following hypotheses: versus . The test statistic is: . Compliance with the claim is shown if , where is the α-th percentile of a chi square distribution with N dfs (α = 0.05).  | *Use the same boilerplate language* |
| 5 | Specify minimum requirements for a precision profile – **compliance endpoint (2)** | Estimate RC separately for the 15 smallest tumors and for the 16 largest. must be < δ for each group in order for this conformance requirement to be met..  |  |
| ***Test for Fixed Bias*** *(This is important for Cross-sectional claims, and for Longitudinal claims when different imaging methods are allowed at the two time points.)* |
| 6 | Identify the test data for evaluating actor’s bias. Another option is to require the actor to generate the test data. | The previously designed FDA Lungman phantom will be used. It includes a range of lesion characteristics (various sizes, densities, shapes).  | N/A |
| 7 | Specify minimum # of observations needed to evaluate bias. See Table 3 below for guidance. | Lungman phantom has 42 distinct target tumors. If each tumor is measured twice (N=82), then according to Table 3 the study will be able to put a tight (+1%) CI around the bias. | N/A |
| 8 | State the methods for estimating actor’s bias  | For each case, calculate the QIB measurement (denoted Yi), where *i* denotes the *i*-th case. Calculate the % bias: , where Xi is the measurand value (i.e. true value). Over N cases estimate the population bias: . The estimate of variance of the bias is . | N/A |
| 9 | Specify the test to assess conformance to the claim – **compliance endpoint (3)** | The 95% CI for the bias is , where is from the Student’s t-distribution with =0.025 and (N-1) degrees of freedom. If the absolute value of smallest and largest values in CI are <5%, then performance requirement is met. Alternatively, Profile authors may choose to allow actors to take advantage of good precision and have a little extra bias so that total error (i.e. bias and imprecision) meets requirements for precision [1].  | N/A |
| 10 | Specify the minimum requirements for providing a bias profile – **compliance endpoint (4)** | Stratify the cases by shape. For each stratum estimate the population bias. The estimated *popbias* must be < 5% for each stratum in order for this conformance requirement to be met [2].  | N/A |
| ***Test for Linearity*** |
| 11 | Identify the test data for evaluating actor’s linearity. Another option is to require the actor to generate the test data. | The previously designed FDA Lungman phantom will be used.  |  |
| 12 | Specify the minimum # of observations needed to evaluate linearity | 5-10 nearly equally-spaced measurand values (*X*) should be chosen with 10 observations per measurand value. |  |
| 13 | State the methods for estimating the regression line  | For each case, calculate the QIB measurement (denoted Yi), where *i* denotes the *i*-th case. Fit an ordinary least squares (OLS) regression of the Yi’s on Xi’s. A quadratic term is first included in the model to rule out non-linear relationships: . If then a linear model should be fit: , where R-squared (R2) >0.90. Let denote the estimated slope. Calculate its variance as , where is the fitted value of Yi from the regression line and is the mean of the true values. | *Use the same boilerplate language* |
| 14 | Specify the test to assess conformance to the claim – **compliance endpoint (5)** | The 95% CI for the slope is . If the smallest value in CI is greater than 0.95 and the largest value in CI is less than 1.05, then this conformance requirement is met [2]. | *Use the same boilerplate language* |

**Table 2: Sample Size for Test of Precision Using RC\***

|  |  |
| --- | --- |
| **(θ/δ)2** | **# cases needed** |
| 0.1 | 4 |
| 0.2 | 7 |
| 0.3 | 11 |
| 0.4 | 17 |
| 0.5 | 29 |
| 0.6 | 51 |
| 0.7 | 102 |
| 0.8 | 256 |

 \* for 80% power, where δ is the RC in the claim and θ

is the actor’s RC.

**Table 3: Sample Size for Evaluating Bias**

|  |  |
| --- | --- |
|  | **Half-Width of 95% CI for Bias** |
|  | **+ 1%** | **+ 2%** | **+ 3%** | **+ 4%** | **+ 5%** |
| **Varb**\***=5%** | 22 | 8 | <5 | <5 | <5 |
| **Varb=10%** | 42 | 13 | 7 | <5 | <5 |
| **Varb=15%** | 61 | 17 | 9 | 7 | <5 |
| **Varb=20%** | 80 | 22 | 12 | 8 | 6 |
| **Varb=25%** | 99 | 27 | 14 | 9 | 7 |

\*The variance is represented here as the variance (from step 8) divided by the bias.

**References:**

[1] Obuchowski NA, Buckler A, Kinahan P, Chen-Mayer H, Petrick N, Barboriak DP, Bullen J,

Barnhart H, Sullivan DC. Statistical Issues in Testing Conformance with the Quantitative

Imaging Biomarker Alliance (QIBA) Profile Claims. *Academic Radiology* 2016; 23: 496-506.

[2] Obuchowski NA, Bullen J. Quantitative Imaging Biomarkers: Coverage of Confidence Intervals

for Individual Subjects. In progress.