Table 1: Nancy’s Table 4 from document ComplianceMarch252015-NP.docx and is part of the current version of Profile in Table 3.6.2-2 (in part).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Allowable Bias** | **Upper 95% CI for RC** | **Conservative estimate of wCV2** | **wCV2 + bias2** |
| 5% | <7.2% | 6.7 | 5.9 | 57.7 |
| 6% | <7.0% | 8.0 | 8.3 | 57.3 |
| 7% | <6.8% | 9.4 | 11.6 | 57.8 |
| 8% | <6.5% | 10.7 | 15.0 | 57.3 |
| 9% | <6.3% | 12.0 | 18.8 | 58.5 |
| 10% | <5.9% | 13.4 | 23.3 | 58.1 |
| 11% | <5.5% | 14.7 | 28.2 | 58.5 |
| 12% | <5.1% | 16.0 | 33.5 | 59.5 |
| 13% | <4.5% | 17.4 | 39.3 | 59.6 |
| 14% | <3.8% | 18.7 | 45.6 | 60.0 |
| 15% | <2.8% | 20.0 | 52.3 | 60.1 |
| 16% | <1.2% | 21.3 | 59.1 | 60.5 |
| 21% | none |  |  | 57.47 |

**Two-side analyses**

Table 2: Update on Table 1 above using a fixed target RMSE based on the RCp=21% and using log transformed data to calculate the upper bound (UB) and the allowable bias for each subgroup (two sided). (From Qin Li)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| RCp | wCV (log)  (eq.1) | wCV UB (log)  (eq.2) | Allowable bias  (log) (eq.3) | Allowable bias  (pct) (eq.4) | wCV2+bias2  (log) / RMSE (pct) |
| 5% | 0.0176 | 0.0234 | 0.0647 | 6.7% | 0.0047 / 7.1% |
| 6% | 0.021 | 0.028 | 0.0629 | 6.5% | 0.0047 / 7.1% |
| 7% | 0.0244 | 0.0325 | 0.0607 | 6.3% | 0.0047 / 7.1% |
| 8% | 0.0278 | 0.0369 | 0.0581 | 6.0% | 0.0047 / 7.1% |
| 9% | 0.0311 | 0.0414 | 0.055 | 5.7% | 0.0047 / 7.1% |
| 10% | 0.0344 | 0.0457 | 0.0514 | 5.3% | 0.0047 / 7.1% |
| 11% | 0.0377 | 0.0501 | 0.0472 | 4.8% | 0.0047 / 7.1% |
| 12% | 0.0409 | 0.0544 | 0.0422 | 4.3% | 0.0047 / 7.1% |
| 13% | 0.0441 | 0.0587 | 0.036 | 3.7% | 0.0047 / 7.1% |
| 14% | 0.0473 | 0.0629 | 0.0279 | 2.8% | 0.0047 / 7.1% |
| 15% | 0.0505 | 0.0671 | 0.0154 | 1.5% | 0.0047 / 7.1% |
| 16% | 0.0536 | 0.0712 | negative | negative | 0.0051 |
| 21% | 0.0688 |  |  | 0% | 0.0047 |

In table. 1, the target RMSE = 7.1% or MSE = 0.0688^2 in log space

(RCp = 21% 🡪 RC = 0.1906 🡪 wCV = 0.0688 trade for RMSE in log space 🡪 RMSE = 7.1%).

For the calculation,

* (eq.1) wCV = RC/2.77; RC = log(1+RC\_pct/100);
* (eq.2) wCV 95% CI upper bound = sqrt(31\*wCV2/chi2(0.025, 31));
* (eq.3) allowable bias = sqrt(0.0047-wCV\_ub2)
* (eq.4) bias\_pct = (exp(bias)-1)x100

Table 3: Table of allowable bias for each RCp subgroup based on the MSE for any shape (spherical, ovoid, lobulated) reaching 110% of total RMSE. Note, total RMSE still must meet the target but we’re allowing some flexibility for within each shape subgroup (two-side). See Section 3.6.2 Specifications subsection in the Profile for more details. (From Qin Li)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| RCp | wCV (log) | wCV UB (log) | Allowable bias for RMSE 7.1% (pct) | Allowable subgroup bias  (pct) for RMSE 7.8% | (Bias\_sub-Bias\_all)/Bias\_all |
| 5% | 0.0176 | 0.0234 | 6.7% | 7.4% | 10.2% |
| 6% | 0.021 | 0.028 | 6.5% | 7.2% | 10.8% |
| 7% | 0.0244 | 0.0325 | 6.3% | 7.0% | 11.5% |
| 8% | 0.0278 | 0.0369 | 6.0% | 6.7% | 12.5% |
| 9% | 0.0311 | 0.0414 | 5.7% | 6.4% | 13.8% |
| 10% | 0.0344 | 0.0457 | 5.3% | 6.1% | 15.7% |
| 11% | 0.0377 | 0.0501 | 4.8% | 5.7% | 18.3% |
| 12% | 0.0409 | 0.0544 | 4.3% | 5.3% | 22.5% |
| 13% | 0.0441 | 0.0587 | 3.7% | 4.8% | 29.8% |
| 14% | 0.0473 | 0.0629 | 2.8% | 4.1% | 46.1% |
| 15% | 0.0505 | 0.0671 | 1.5% | 3.4% | 117.9% |
| 16% | 0.0536 | 0.0712 | negative | 2.3% |  |
| 21% | 0.0688 |  | 0% | - | - |

**One-side analyses**

Table 4: Update on Table 2 above using a fixed target RMSE based on the RCp=21%, and using log transformed data to calculate the upper bound (UB) and the allowable bias for each subgroup (one-side). (From Qin Li).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| RCp | wCV (log)  (eq.1) | wCV UB (log)  (eq.2) | Allowable bias  (log) (eq.3) | Allowable bias  (pct) (eq.4) | wCV2+bias2  (log) / RMSE (pct) |
| 5% | 0.0176 | 0.0223 | 0.0651 | 6.7% | 0.0047 / 7.1% |
| 6% | 0.021 | 0.0267 | 0.0634 | 6.5% | 0.0047 / 7.1% |
| 7% | 0.0244 | 0.0310 | 0.0615 | 6.3% | 0.0047 / 7.1% |
| 8% | 0.0278 | 0.0352 | 0.0591 | 6.1% | 0.0047 / 7.1% |
| 9% | 0.0311 | 0.0394 | 0.0564 | 5.8% | 0.0047 / 7.1% |
| 10% | 0.0344 | 0.0436 | 0.0532 | 5.5% | 0.0047 / 7.1% |
| 11% | 0.0377 | 0.0478 | 0.0495 | 5.1% | 0.0047 / 7.1% |
| 12% | 0.0409 | 0.0519 | 0.0452 | 4.6% | 0.0047 / 7.1% |
| 13% | 0.0441 | 0.0559 | 0.0401 | 4.1% | 0.0047 / 7.1% |
| 14% | 0.0473 | 0.0600 | 0.0337 | 3.4% | 0.0047 / 7.1% |
| 15% | 0.0505 | 0.0640 | 0.0253 | 2.6% | 0.0047 / 7.1% |
| 16% | 0.0536 | 0.0679 | 0.0109 | 1.1% | 0.0047 / 7.1% |
| 21% | 0.0688 |  |  | 0% | 0.0047 |

In table. 1, the target RMSE = 7.1% or MSE = 0.0688^2 in log space

(RCp = 21% 🡪 RC = 0.1906 🡪 wCV = 0.0688 trade for RMSE in log space 🡪 RMSE = 7.1%).

For the calculation,

* (eq.1) wCV = RC/2.77; RC = log(1+RC\_pct/100);
* (eq.2) wCV 95% CI upper bound = sqrt(31\*wCV2/chi2(0.05, 31));
* (eq.3) allowable bias = sqrt(0.0047-wCV\_ub2)
* (eq.4) bias\_pct = (exp(bias)-1)x100

Table 5: Table of allowable bias for each RCp subgroup based on the MSE for any shape (spherical, ovoid, lobulated) reaching 110% of total RMSE. Note, total RMSE still must meet the target but we’re allowing some flexibility within each shape subgroup (one-side). (From Qin Li)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| RCp | wCV (log) | wCV UB (log) | Allowable bias for RMSE 7.1% (pct) | Allowable subgroup bias  (pct) for RMSE 7.8% | (Bias\_sub-Bias\_all)/Bias\_all |
| 5% | 0.0176 | 0.0223 | 6.7% | 7.4% | 10.4% |
| 6% | 0.021 | 0.0267 | 6.5% | 7.3% | 10.9% |
| 7% | 0.0244 | 0.0310 | 6.3% | 7.1% | 11.5% |
| 8% | 0.0278 | 0.0352 | 6.1% | 6.8% | 12.4% |
| 9% | 0.0311 | 0.0394 | 5.8% | 6.6% | 13.6% |
| 10% | 0.0344 | 0.0436 | 5.5% | 6.3% | 15.1% |
| 11% | 0.0377 | 0.0478 | 5.1% | 5.9% | 17.2% |
| 12% | 0.0409 | 0.0519 | 4.6% | 5.6% | 20.3% |
| 13% | 0.0441 | 0.0559 | 4.1% | 5.1% | 25.3% |
| 14% | 0.0473 | 0.0600 | 3.4% | 4.6% | 34.2% |
| 15% | 0.0505 | 0.0640 | 2.6% | 4.0% | 55.5% |
| 16% | 0.0536 | 0.0679 | 1.1% | 3.2% | 193.5% |
| 21% | 0.0688 |  | 0% | - | - |

**Summary**

Our proposal for updating Table 3.6.2-2 in the Profile would be to use the one-side limits from Table 4 such that the following table would be included in the profile:

**Table 3.6.2-2:   
Allowable Tumor Volume %Bias based on Repeatability Coefficient**

|  |  |  |
| --- | --- | --- |
| **Repeatability Coefficient p** | **Allowable Overall %Bias**  **RMSE Target: 7.1%** | **Allowable Shape Subgroup %Bias**  **RMSE Target: 7.8%** |
| 5% | <6.7% | <7.4% |
| 6% | <6.5% | <7.3% |
| 7% | <6.3% | <7.1% |
| 8% | <6.1% | <6.8% |
| 9% | <5.8% | <6.6% |
| 10% | <5.5% | <6.3% |
| 11% | <5.1% | <5.9% |
| 12% | <4.6% | <5.6% |
| 13% | <4.1% | <5.1% |
| 14% | <3.4% | <4.6% |
| 15% | <2.6% | <4.0% |
| 16% | <1.1% | <3.2% |
| 21% | - | - |