Coronavirus Standards Working Group Meeting Summary

Dear Colleagues —

It was great to work together this morning to dive into analysis of our Viral RNA Harmonization Study together -- thanks all for your careful study of the data and results in the dashboard. And thanks all for your kind words about our web-hosted software tool. It has been a labor of devotion to develop. My hope is being realized: giving everyone collaborative and transparent access to their own review and consideration of the data. Technology advances have made this practical, in particular, using the R statistical analysis language with the R Shiny web app development platform.

I continue to make changes to the code to add features that let us explore the data. This afternoon I added a raw data browser, which should be helpful for all labs to use to get to the bottom of some of the anomalies we discussed this morning.

The analysis dashboard is linked here at a stable web link.

Our meeting was recorded and can be watched here.

As noted this morning

- all data have been received from 13/14 labs
- calibration curves are now fitted with inverse variance weighting
- dilutions of the Asuragen sample have been updated in the data files, and should be correct
    - this can be confirmed in the raw data browser
- the calibration approach for the single-point NMI results has been changed to a simple proportional scaling of dPCR results to the reported copy number value of the International Standard
- other anomalies in the data files have been updated

Critical & important next steps

- David and I need to comb through the submitted metadata to get the handling right
    - for instance, we have a 2x bias in our analysis of the MUSC data, as the WHO IS was diluted 2x before being used to make the calibration curves (in order to accommodate the volume requirement of the assay platform).
- Critical review of the units of value assignment
    - is our application of the International Standard as a reconstituted calibration material establishing the calibration in (International Units)/(reconstitution volume)? we calculating a concentration
- We must consider how to summarize multiple targets from a single lab
- We should consider where samples were measured in batches (for instance, in different plates or on different days) and test for batch effects and analyze appropriately
    - NIST & NML measured on multiple days, and if there is evidence of a Day Effect, we can do per-day calibration
- We must consider how to summarize data from multiple labs to assign values the 8 materials in the study
    - this summary technical approach must consider the variation of the results to establish an associated measurement uncertainty
    - we will reach out to colleagues at NIST and NML to help

I look forward to seeing many of you at our workshops next week to consider a Standards Architecture for Pathogen Genomic Surveillance. The CSWG will meet again on June 18.

Cheers and stay safe!
Marc

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