5-14-13 Scientific Advisory Committee DNA/Biology Subcommittee Meeting, 8:30 am

Members present: Brad Jenkins (BCJ), Lisa Schiermeier-Wood (LCS), Susan Greenspoon (SG), Dave Barron, Carl Sobierallski, John Butler (JB), John Planz, Stephanie Merritt (SEM), Gail Jaspen, Grey Collins, Deborah Collard-taking minutes.

Minutes:

8:30 am start, Mr. Jenkins (BCJ) from VA Department of Forensic Science (DFS) gives introduction, explains the information in the packets for this meeting and SAC later this morning (SAC starts at 10:00 am).

At the last SAC meeting, it was agreed that the subcommittee would meet to discuss the 2 agenda items: 1) DFS True Allele (TA) Validation and 2) DFS Armed Xpert (AX) Validation

Both studies are looking into DNA mixtures

There are 2 TA validation pieces, one version is from Dr. Perlin using DFS data and case information. Dr Perlin offers his suggestions in this study. The other validation is an internal study completed at DFS; Susan Greenspoon (SG) will talk about this study this morning. This Validation Study is DFS's interpretation of TA.

John Butler (JB) asks whether Dr. Perlin has submitted his study to a peer review journal? BCJ responds that yes it has been submitted but not yet published. DFS may issue an internal report with TA data in the future.

SG begins slide presentation, see handout, slide 1.

JB asks about the 111 comparisons on slide one (see handout) does that equal 111 likelihood ratio? SG explains the derived genotypes, a 3 person mixture will have 3 person likelihood, and each mixture is considered a comparison (slide 1).

SG explains slide 2- Sensitivity, see handout.

Slide 3, see handout, Cybergenetics +DFS data on specificity, comparing reported genotypes to reference genotypes in the 71 unrelated cases

Lots of info on Specificity slide, see handout, x axis is likelihood ration (LR), above are averages generated, green=cpi, red=mod cpi, blue=TA. For 72 cases the TA runs the gauntlet, from 0 to extreme. Cpi in green is confined to smaller range, mod cpi even smaller range. Left side of graph is frequency of nothing recorded; the data doesn't fit the criteria. For TA the nothing reported is smaller. This is a comprehensive summary slide.

BCJ talks about no stochastic threshold, later with new guidelines, a stochastic threshold is developed. BCJ discusses options where DFS could not do statistics based on data at every locus being below stochastic threshold. The idea was - Let's try the TA system to see what data we can get for our cases.

JB asks, Is it apples to oranges? BCJ explains It is but Dr. Perlin considers cpi as likelihood ratios. Question asked, is that his idea alone? BCJ answers, That's how he presents it in his publications.

Question asked, is the stochastic threshold modified? Correct, yes that is what it is.

SG explains from the Specifity slide, see handout, that the study involved taking genotypes from one case at a time and comparing that to reference samples from other cases and deriving likelihood ratios (LR). TA can use multiple references, multiple suspects, we like that about TA, the negative log likelihood ratio supports the negative alternate hypothesis.

DFS validation study, see handout, used 17 single source samples, 18 two person mixtures, 10 three person mixtures, and 7 four person mixtures (see slide) testing the TA process; if it exhibited allelic drop out, the accuracy of TA process, looked at limitations of TA process, what statistics were generated, and the specificity of TAs reproducibility.

Summary of Results, see slide in handout, SG explained results in slide, SG answers a question about hetero zygote drop out, explains how profiles are considered as possibilities, TA provides a detailed report listing all the probabilities of genotypes, sometimes there are multiple pages for each loci, TA considers each loci, if locus is completely dropped out, then it doesn't consider it at all

Lisa Schiermeier-Wood (LCS) explains it is possible to upload your own probabilities, for TA to consider.

SG answers a question about reproducibility, did you repeat the work? Generally the standard deviations are pretty tight; there are larger standard deviations if the mixture is 50/50, 3 and 4 person mixtures give larger standard deviations.

SG continues to explain Results slide, comparisons with relatives: then found 2 mixtures showed observable logs to relative. Question from JB about, are you going to establish how many runs per sample? BCJ answers, yes we will set up standards to produce reproducible results, we are thinking in the 5 run range to produce duplicate samples, to see the replicate we need. BCJ: we can't run too many runs and be done in a reasonable amount of time. LCS states in the validation paper you see how many runs were done. SG explains we have criteria to determine if the runs are usable, a variety of metrics are used.

SG goes back to Results slide, see handout, and the use of assumed knowns, in general when you use an assumed known the log likelihood ratios are increased. 4 person mixtures in TA were reproducible and had consistent results. Cycles for simple mixtures were 25,000, for 4 person mixtures cycles were at 100,000 cycles.

SG continues to explain Results slide, see handout, one out of 7 was inconclusive results. Small comparison with relatives explained in slide.

SG moves on to explain Specificity slide with large table, see handout. SG Explains that one was not reproducible. SG was very pleased with specificity test. 3 & 4 person mixtures chosen were difficult mixtures, with lots of low level contributors. The predominant contributor was always picked up.

LCS explains that there were a handful of samples that were at zero log which would be where inconclusive would fall. JB asks question about inconclusive, BCJ answers that is h=where the inconclusive fall, LCS explains "there is no statistical support reported" is how the actual report states the results.

SG moves on to next slide, computation times, see handout. Analysis times take longer for complex mixtures in an 8 parallel processor, approx times, for each single run, BCJ would set up both runs at one time for reproducibility. SG states, that does not guarantee that runs are usable. A question about making decision on the data and inconclusiveness before you spend the time to repeat runs is asked.

BCJ answers, DFS interprets 2 & 3 person mixtures, 4 person mixtures will not be interpreted. LCS gives verbiage used… (check tape for exact statement).

SG moves onto Summary of validation slide, see handout, SG explains slide, assumed knowns, results close relatives might generate. A question is asked about were relatives sons? Yes, it was easier to generate the sons instead of sibling. SG continues to explain; Specificity…1/35, positive match score only, see hand out.

BCJ asks if there are any other questions for SG? Then introduces LCS.

LCS to discuss TA training and implementation at DFS, team is out of central lab. Explains team from slide, see hand out.

LCS describes how the training worked, see handout. LCS explains an overview of training on software then continued onto operator 1 training, see handout. All training was provided by Cybergenetics. Training over the summer, next slide in handout, in reporter training DFS practices testifying.

LCS explains next slide, see handout, how she and SG both gave TA presentations to peer groups, Dr Perlin has completed reports on cases, DFS has offered to prepare attorneys, as a courtesy, on TA cases before they begin to talk with Dr. Perlin and need to start paying his consulting fees.

LCS describes next slide implementation, see handout, DFS does not routinely interpret 4 person mixtures, we write them up as unknown # of contributors this was not calculated. DFS continues with human interpretation before we use TA. BCJ adds, if we have eliminated some one already we will not sent the case for TA calculations. LCS continues to explain slide.

- tape recording the meeting is turned over

LCS discusses time required to get TA results, see handout TrueAllele Implementation slide 1.

LCS continues with TrueAllele Implementation slide 2, see handout, what DFS will NOT be doing; DFS will not be doing joint calculations.

LCS explains Implementation Logistics slide, see handout, the process, and how it will work at DFS.

A question from the committee is asked about peer review? How is it done, by hand calculations? LCS explains peer review will look at concordance between runs, check requests, check data and usefulness, identify useful data, check concordances. LCS- how do we keep this data? Dr Perlin will help with model on what is provided on discovery in cases. A question is asked about what does Dr. Perlin provide now for discovery? LCS responds that we send case notes; you can also make an appt with examiner to view other data. Stephanie Merritt (SEM) responds to help support answer. SEM states, DFS does not provide software with electronic data, data only not soft ware to read it, SEM assumes the defense experts must own software to view results, the VA code states that DFS can have records reviewed here at DFS, this is allowed by VA code, Dr. Perlin has been providing paper records and some electronic records, SEM explains how DFS provides Dr. Perlin's documents for Subpoena *Duces Tecum*.

LCS discusses ways to save the data so the files cannot be changed. BCJ has discussed with Dr. Perlin how to provide electronic data to view here at DFS on computer. BCJ explains that examiners will review 5 or 6 criteria in technical peer review, how variable the analysis can or cannot be, examiners will be proficiency tested with TA, and DFS will send data to TA to confirm DFS findings.

BCJ discusses the next phase for DFS to start writing a manual for TA, to define how many runs DFS will perform per case in the manual, we welcome your comments. Let's set a date in June for feedback from the three of you. All to send comments to JB and then he then sends them directly to BCJ. Call BCJ with questions and he will direct you to the right person to explain. Can't have the three of you talking together without the committee. JB wants to know more about the peer review to be done. JB would like to see the papers written up for peers to understand the process. SG explains DFS goes into that quite a bit in the validation study in material and methods we show examples of histograms and what the distributions are, see the amount of sampling, shows the good quality run and what was not useful, shows examples of genotype concordance, TA uses different shades of blue which complicates the comparison, shows dominant contributor, SG shows one good run and one not usable run, you can see the difference, shows the consistency and reproducibility, good runs are assessed as good quality run, defined the metrics in the paper. Looking for reproducibility within 2 logs.

SG to show committee members the standard deviations in the Validation study notebooks.

BCJ briefly discusses Armed Xpert validation work. Then asks, does the third week in June sound possible to get comments back on validation of TA from committee?

BCJ explains there is one more piece of validation for AX. Replacement for population statistics, we can do modified random match probability. Described in SWGDam document, for single allele below stochastic threshold, using it in 2 person mixtures to do unrestricted rnb? DFS is validating a mass ratio approach, to get more usable data; we are in the process of validating that. Last phase is peek high ratio data, last piece for validation. We are now moving our resources onto AX. DFS to use own allelic frequency data in soft ware program. A question is asked about whether or not AX is to be used for day to day calculations in lab? Yes exactly, and TA is for an expert team.

BCJ asks for any other questions. The committee would like to see data on TA and see what data looks like in order to understand what we are looking at. Can we get a pdf of one of them? LCS invites committee members to come upstairs after meeting to look at real data.

JB confirms you want committee feedback in the beginning of June. Send draft of procedures manual when ready. BCJ- we can also send additional studies is you want to see those.

Thank you for coming- BCJ

JB reminds the committee that his turn on SAC is over in June, asks for the committee to share data with Mike Colwell who will be replacing him.

SG to show committee members DFS data in the Validation Study notebooks.

Meeting concluded at approximately 9:50 am.