Appendix

We fit models representing three diagnostic tests in two populations to estimate the posterior distribution of each tests' sensitivity and specificity (ELISA, RBT, CFT). The data is represented as a vector of test results from n_1=161 and n_2=220 observations, where the counts of test results in each population are assumed to follow a multinomial distribution (Table 3). The model assuming conditional independence also assumes that test accuracy is constant across populations and that the true infection prevalence differs between populations. This model requires 8 parameters (Se_E, Se_R, Se_C representing ELISA, RBT and CFT test sensitivity, respectively; Sp_E, Sp_R, Sp_C representing test specificity; p_i, p_{i2} representing prevalence) and results in the following multinomial cell probabilities:

$$\Pr(\text{ELISA +, RBT+, CFT+}) = p_i(Se_E\, Se_R\, Se_C) + (1-p_i)((1-Sp_E)(1-Sp_R)(1-Sp_C))$$

$$\Pr(\text{ELISA +, RBT+, CFT-}) = p_i(Se_E\, Se_R(1-Se_C)) + (1-p_i)((1-Sp_E)(1-Sp_R)Sp_C)$$

with similar extensions for the remaining probabilities. Models that adjust for correlation among test outcomes require additional parameters to represent dependence between each test's sensitivity and specificity, such that six additional parameters are required to represent conditional dependence between all three tests (covariance between test sensitivity, a_{ER}, a_{EC}, a_{RC}, and specificity b_{ER}, b_{EC}, b_{RC}). The fully dependent model is non-identifiable given the data and the number of parameters. As a result, we use prior assumptions and model selection to add constraints on the model's structure and ensure identifiability (Berkvens et al., 2006). To compare the fit of models assuming different amounts of conditional dependence, we used model selection was based on Deviance Information Criteria (DIC). We also calculated conditional correlations between tests because when tests are highly accurate despite measuring the same biological response (Hui and Walter, 1980) or when correlations are low (represented by a

conditional correlation ≤0.2), independence may also be appropriate (Georgiadis et al., 2003). Although these tools clarify the importance of model assumptions and prior information (Menten et al., 2008), models with similar fits to the data may still result in different estimates (Albert and Dodd, 2004). We, therefore, explore the effects of model selection on the sensitivity and specificity estimates by reporting results from models assuming both conditional independence and dependence between tests (van Smeden, 2014; Supplement Table S1).

Prior distributions for diagnostic test sensitivity and specificity were represented as beta distributions and calculated in the program, Beta Buster (http://www.epi.ucdavis.edu/diagnostictests/betabuster.html). We set the mode of the beta distribution as the estimates generated by a meta-analysis of brucellosis test validations from the European Union (Grenier et al., 2009) and the 5^{th} percentile of the distribution as the lowest published estimate of test accuracy (Nielsen, 2002). The lowest published estimate for ELISA accuracy was significantly higher than estimates for the RBT and CFT (92.5%). To represent our uncertainty in applying this sensitivity estimate, we avoid strong prior information by setting the 5^{th} percentile of the beta distribution at 60% (Table 1) and exploring the consequence of this assumption with a sensitivity analysis. We used uniform reference priors for the conditional dependence parameters bounded by the range of possible values given test sensitivity and specificity (Toft et al., 2007) and the population prevalence was defined based on published serological surveys of the Kruger National Park buffalo population (Chapparo et al., 1990).

All latent class models were run with WinBUGS and the R2WinBUGS package (Sturtz et al., 2005) in R (R Core Team, 2012). WinBUGS uses Markov Chain Monte Carlo (MCMC) sampling to obtain the joint posterior distribution of the model (Spiegelhalter et al., 2000). WinBUGS code for the final model representing covariance between the ELISA and CFT is

47 displayed in Supplement 2. Models were run with two chains and 100,000 iterations were
48 performed for posterior inference after discarding the first 50,000 samples of the MCMC chain
49 to allow convergence. Convergence was visually assessed with trace plots and with the Gelman
50 and Rubin diagnostic (Gelman and Rubin, 1992). Convergence diagnostics were assessed with
51 the coda package in R (Plummer et al., 2006).

52

Supplementary Material

Supplement Table S1. Comparison of model fit based on DIC values. In the model assuming full conditional dependence, the parameter representing conditional dependence between the RBT and CFT test sensitivity and the parameter representing conditional dependence between the ELISA and RBT test specificity were not identifiable, but estimates of ELISA sensitivity and specificity were separable and comparable to smaller models. Therefore, model selection based on DIC was used select a plausible model for the data (in bold). 95% Bayesian credible intervals for ELISA sensitivity (ELISA-SE) and ELISA specificity (ELISA-SP) are shown for each model. The modeled assumptions had a minimal effect on the estimated median sensitivity and specificity. The median estimates of test sensitivity ranged from 92.78 to 96.05 while estimates of test specificity ranged from 85.31 to 88.14.

Model	**DIC**	**ELISA- SE**	**ELISA-SP**
Conditional Independence	63.26	93.74 (87.60- 97.97)	87.09 (83.68- 90.13)
CD between ELISA & CFT	**59.24**	**92.78 (86.94- 97.44)**	**86.98 (83.59- 90.03)**
CD between RBT & CFT	61.31	95.06 (88.25- 99.55)	88.14 (84.09- 98.12)
CD between ELISA & RBT	62.44	92.21 (84.90- 97.25)	84.74 (75.55- 97.20)
CD between EL & RBT, RBT & CFT	60.14	93.19 (81.80- 99.36)	85.31 (75.50- 96.25)
CD between EL & CFT, RBT & CFT	61.77	96.05 (89.09- 99.90)	87.88 (83.85- 97.86)
CD between EL & RBT, EL & CFT	62.79	92.94 (83.87- 98.05)	84.39 (74.91- 88.89)
CD between all sensitivity	61.67	92.18 (83.46-97.29)	87.57 (83.78-97.96)
CD between all specificity	62.07	93.94 (86.51-99.26)	84.64 (75.54-89.09)
CD among all tests	60.19	93.00 (82.10-99.41)	84.18 (74.58-95.15)

Supplement 2. The model structure representing three diagnostic tests and two populations is presented below. This WinBUGS code specifies the model structure and was called into R via the R2WinBUGS package. We represent ELISA, RBT, and CFT sensitivity as se[1], se[2], and se[3], respectively and ELISA, RBT, and CFT specificity as sp[1], sp[2], and sp[3], respectively. Covariance between ELISA and CFT sensitivity and specificity are represented as a12 and b12. Brucellosis prevalence in the Lower Sabie herd is represented as pr and brucellosis prevalence in the Crocodile Bridge herd is represented as pr2. Model structure was modified based work in Rahman et al. (2013) and Toft et al. (2007). Additional R or WinBUGS code for this analysis can be obtained by contacting E. Gorsich (eringorsich@gmail.com).

```
model
{
r[1:8] ~ dmulti(p[1:8], n)
r2[1:8] ~ dmulti(p2[1:8], n2)
p[1] <- pr*(se[1]*se[2]*se[3]+se[2]*a13) + (1-pr)*((1-sp[1])*(1-sp[2])*(1-sp[3])+(1-sp[2])*b13)
p[2] <- pr*(se[1]*se[2]*(1-se[3])-se[2]*a13) + (1-pr)*((1-sp[1])*(1-sp[2])*sp[3]-(1-sp[2])*b13)
p[3] <- pr*(se[1]*(1-se[2])*se[3]+(1-se[2])*a13) + (1-pr)*((1-sp[1])*sp[2]*(1-sp[3])+sp[2]*b13)
p[4] <- pr*(se[1]*(1-se[2])*(1-se[3])-(1-se[2])*a13) + (1-pr)*((1-sp[1])*sp[2]*sp[3]-sp[2]*b13)
p[5] <- pr*((1-se[1])*se[2]*se[3]-(1-se[2])*a13) + (1-pr)*(sp[1]*(1-sp[2])*(1-sp[3])-(1-sp[2])*b13)
p[6] <- pr*((1-se[1])*se[2]*(1-se[3])+se[2]*a13) + (1-pr)*(sp[1]*(1-sp[2])*sp[3]+(1-sp[2])*b13)
p[7] <- pr*((1-se[1])*(1-se[2])*se[3]-(1-se[2])*a13) + (1-pr)*(sp[1]*sp[2]*(1-sp[3])-sp[2]*b13)
p[8] <- pr*((1-se[1])*(1-se[2])*(1-se[3])+(1-se[2])*a13) + (1-pr)*(sp[1]*sp[2]*sp[3]+sp[2]*b13)

p2[1] <- pr2*(se[1]*se[2]*se[3]+se[2]*a13) + (1-pr2)*((1-sp[1])*(1-sp[2])*(1-sp[3])+(1-sp[2])*b13)
p2[2] <- pr2*(se[1]*se[2]*(1-se[3])-se[2]*a13) + (1-pr2)*((1-sp[1])*(1-sp[2])*sp[3]-(1-sp[2])*b13)
p2[3] <- pr2*(se[1]*(1-se[2])*se[3]+(1-se[2])*a13) + (1-pr2)*((1-sp[1])*sp[2]*(1-sp[3])+sp[2]*b13)
p2[4] <- pr2*(se[1]*(1-se[2])*(1-se[3])-(1-se[2])*a13) + (1-pr2)*((1-sp[1])*sp[2]*sp[3]-sp[2]*b13)
p2[5] <- pr2*((1-se[1])*se[2]*se[3]-(1-se[2])*a13) + (1-pr2)*(sp[1]*(1-sp[2])*(1-sp[3])-(1-sp[2])*b13)
p2[6] <- pr2*((1-se[1])*se[2]*(1-se[3])+se[2]*a13) + (1-pr2)*(sp[1]*(1-sp[2])*sp[3]+(1-sp[2])*b13)
p2[7] <- pr2*((1-se[1])*(1-se[2])*se[3]-(1-se[2])*a13) + (1-pr2)*(sp[1]*sp[2]*(1-sp[3])-sp[2]*b13)
p2[8] <- pr2*((1-se[1])*(1-se[2])*(1-se[3])+(1-se[2])*a13) + (1-pr2)*(sp[1]*sp[2]*sp[3]+sp[2]*b13)

#Priors
pr ~ dbeta(2.35, 4.14)
pr2 ~ dbeta(1.96, 2.78)
se[1] ~  dbeta(6.2881, 1.13)
se[2] ~dbeta(1.9348, 1.018)
se[3] ~ dbeta(2.0791, 1.045)
sp[1] ~ dbeta(6.30745, 1.1361)
```

```
105     sp[2] ~ dbeta(8.077, 1.0142)
106     sp[3] ~ dbeta(2.5335, 1.003)
107     ll1 <- max(-(1-se[1])*(1-se[3]), -se[1]*se[3])
108     ul1 <- min(se[1]*(1-se[3]),(1-se[1])*se[3])
109     a13 ~ dunif(ll1,ul1)
110     ll2 <- max(-(1-sp[1])*(1-sp[3]), -sp[1]*sp[3])
111     ul2 <- min(sp[1]*(1-sp[3]),(1-sp[1])*sp[3])
112     b13 ~ dunif(ll2,ul2)
113
114     # correlation between ELISA and CFT
115     cc_a13 <- a13/(sqrt(se[1]*(1-se[1]))*sqrt(se[3]*(1-se[3])))
116     cc_b13 <- b13/(sqrt(sp[1]*(1-sp[1]))*sqrt(sp[3]*(1-sp[3])))
117     }
```