A. IgG

IpaB
$Y = 1.074*X - 0.3623, R^2 = 0.999$

IpaC
$Y = 1.107*X - 0.4766, R^2 = 0.999$

IpaD
$Y = 1.083*X - 0.3957, R^2 = 0.999$

IpaH
$Y = 1.083*X - 0.3182, R^2 = 1.000$

VirG
$Y = 1.057*X - 0.2397, R^2 = 0.999$

S. flexneri 2a LPS
$Y = 1.060*X - 0.2644, R^2 = 0.994$

S. flexneri 3a LPS
$Y = 1.110*X - 0.3398, R^2 = 0.991$

S. flexneri 6 LPS
$Y = 1.041*X - 0.08323, R^2 = 0.987$

S. sonnei LPS
$Y = 1.036*X - 0.1494, R^2 = 0.998$

Log_{10} Calculated concentration (pg/mL)

Log_{10} Expected concentration (pg/mL)

B. IgA

IpaB
$Y = 0.9940*X + 0.004478, R^2 = 0.994$

IpaC
$Y = 1.034*X - 0.1258, R^2 = 0.995$

IpaD
$Y = 0.9814*X + 0.06582, R^2 = 0.998$

IpaH
$Y = 0.9926*X + 0.01340, R^2 = 0.995$

VirG
$Y = 1.002*X - 0.01884, R^2 = 0.997$

S. flexneri 2a LPS
$Y = 1.166*X - 0.6016, R^2 = 0.998$

S. flexneri 3a LPS
$Y = 1.178*X - 0.7340, R^2 = 0.998$

S. flexneri 6 LPS
$Y = 1.059*X - 0.1573, R^2 = 0.994$

S. sonnei LPS
$Y = 1.122*X - 0.3982, R^2 = 0.998$

Log_{10} Calculated concentration (pg/mL)

Log_{10} Expected concentration (pg/mL)
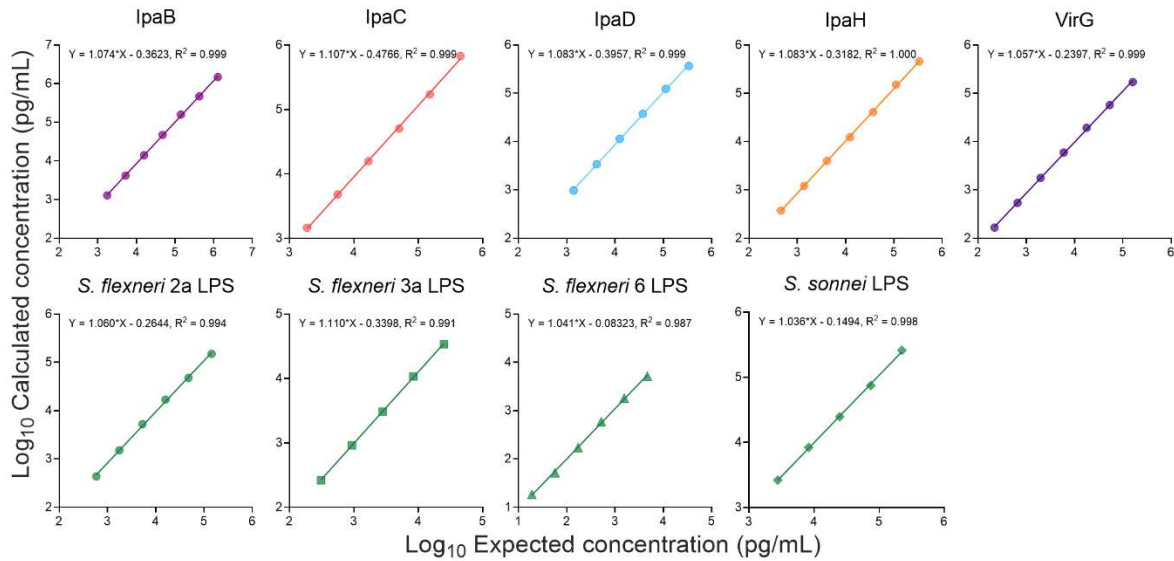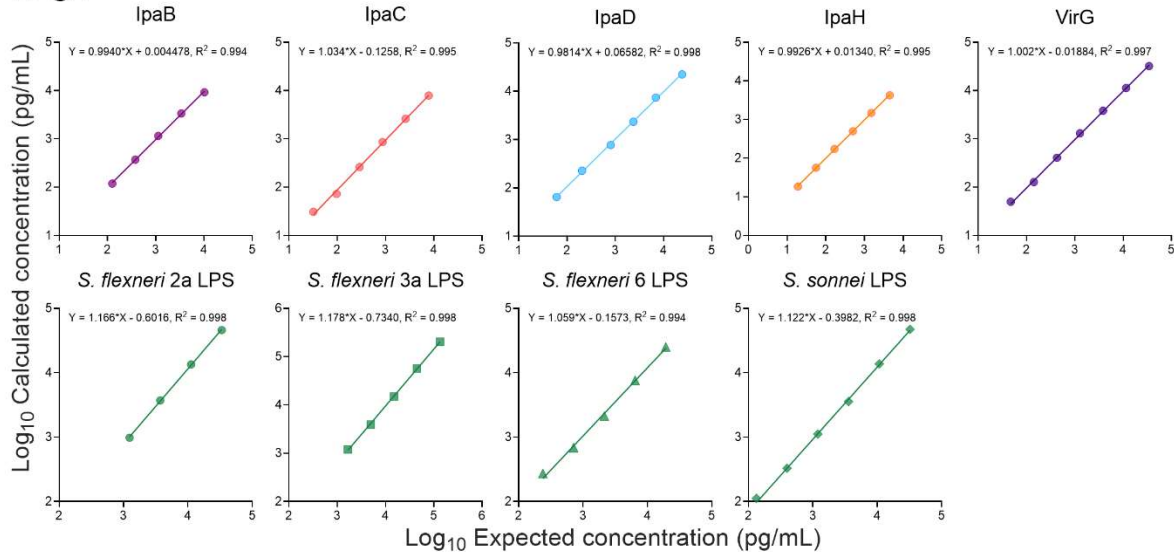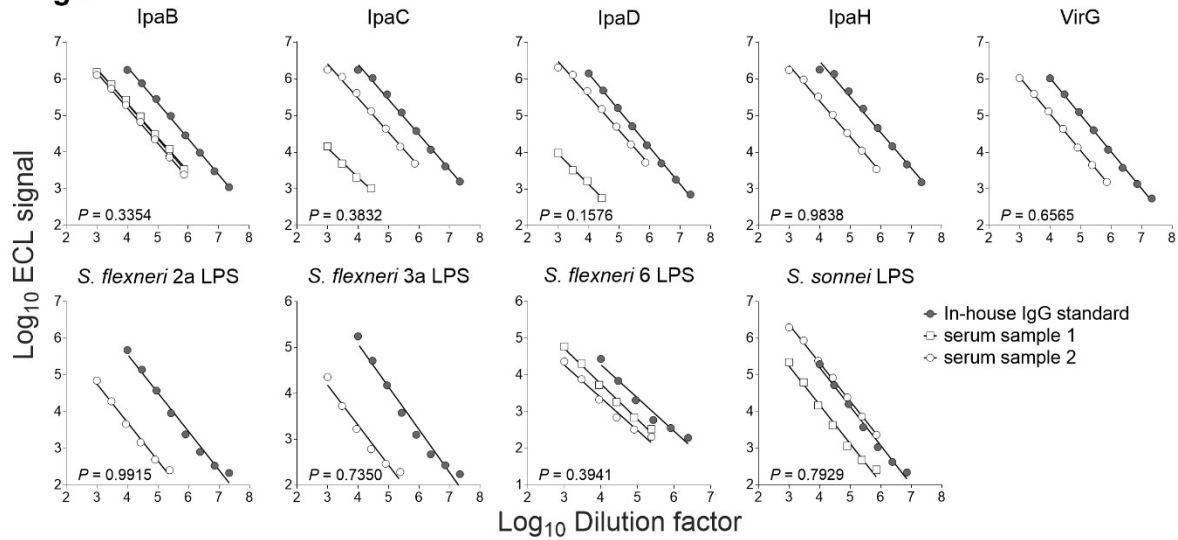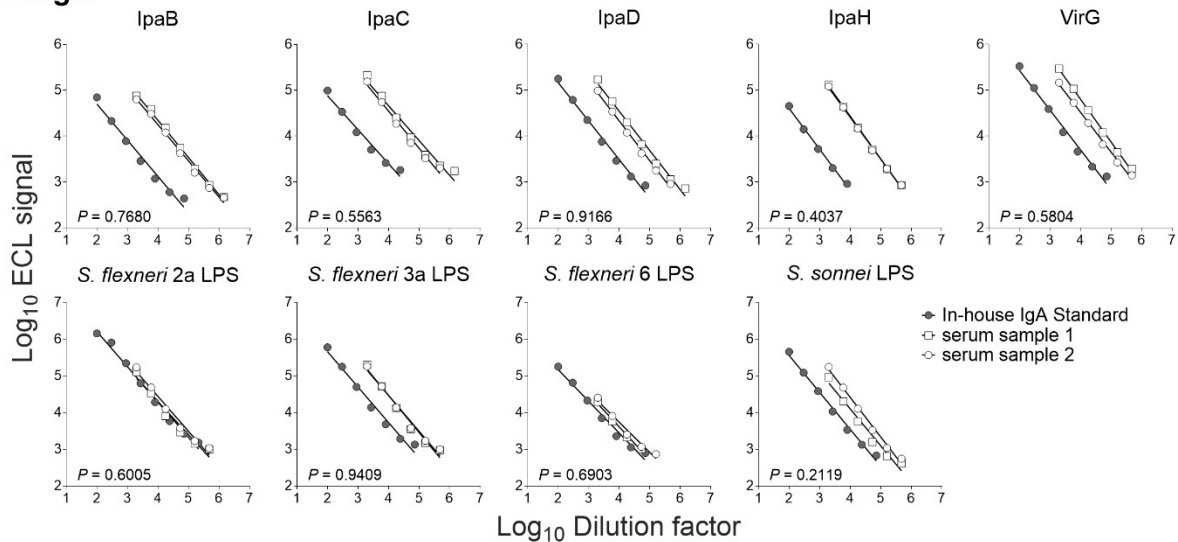
Figure S1. Assay linearity. Representative mock samples generated by dilution of pooled serum controls in negative serum were tested in the MSD IgG (**A**) and IgA (**B**) assay. Log-transformed calculated (y-axis) vs expected (x-axis) antibody concentrations at each dilution were compared. Linear regression curves with the equation and R^2 values for each antigen are shown.

Figure S2. Parallelism. The in-house standards and 2 serum samples from different donors were tested in three-fold serial dilutions in the MSD IgG (**A**) and IgA (**B**) assays. Log-transformed ECL signals were plotted against the dilution factor; linear regression curves are shown for each sample in each graph. Comparisons between the lines showed that the slopes were not significantly different ($P>0.05$).
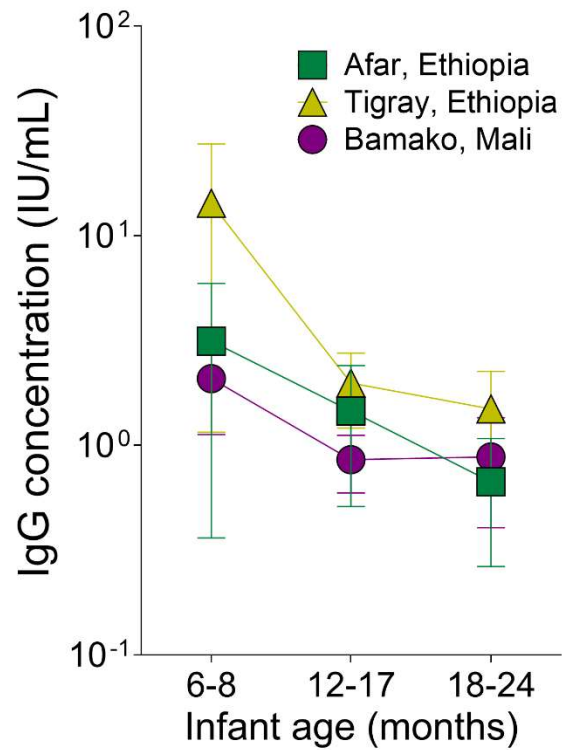
Table S1. Adult cohort characteristics

	Year samples collected	Age range	Sex (M/F)	n
USA (cohort 1)[1]	1993	18-40 years	26/2	28
USA (cohort 2)	2015	22-62 years	14/31	45
Mali[2]	2011	15-39 years	0/18	18
Malawi[3]	2016	17-43 years	0/18	83

[1]Kotloff et al., 1995. Evaluation of the safety, immunogenicity, and efficacy in healthy adults of four doses of live oral hybrid *Escherichia coli- Shigella flexneri* 2a vaccine strain EcSf2a-2. Vaccine 13:495-502.
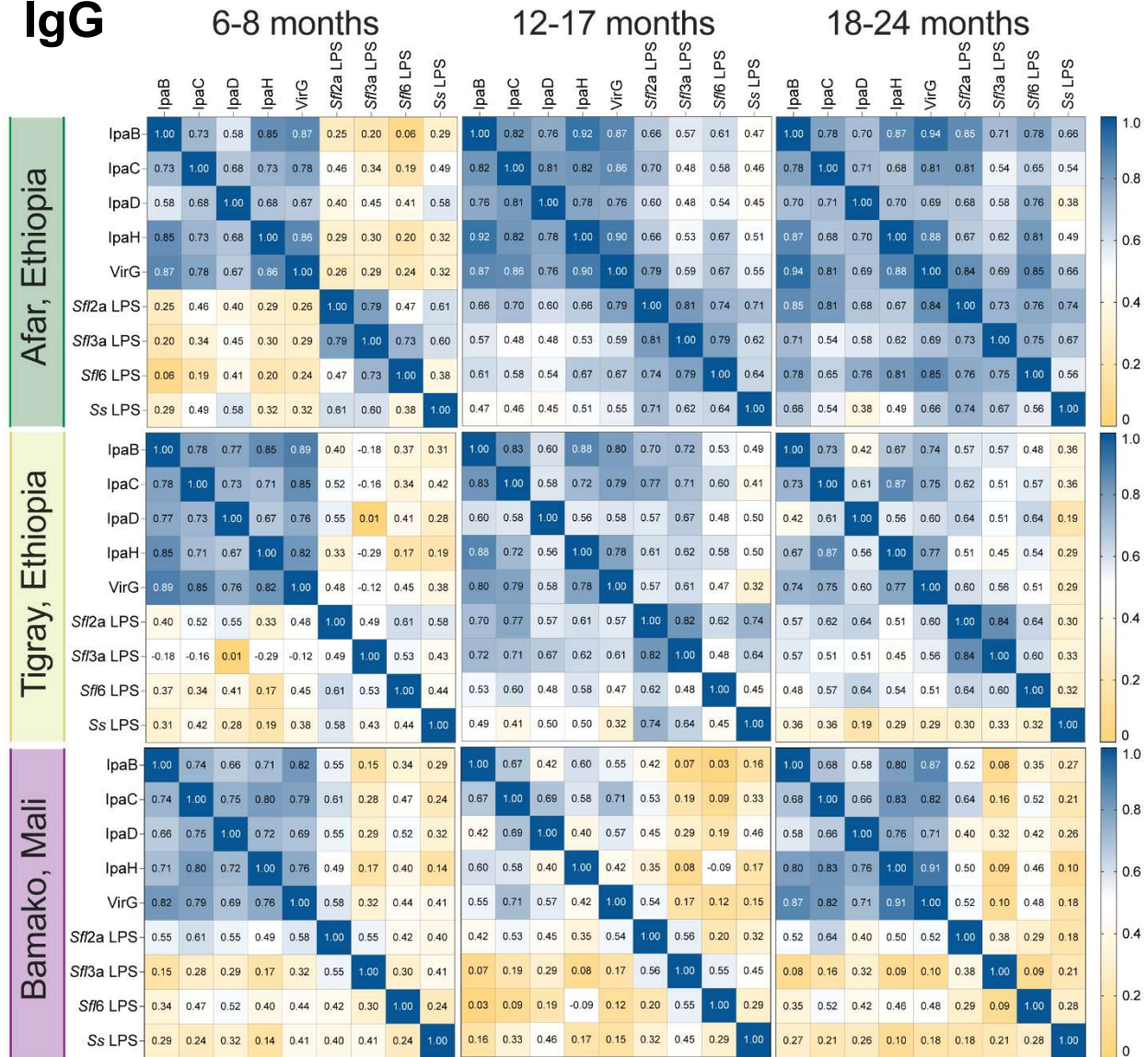
[2]Tapia et al., 2016. Maternal immunisation with trivalent inactivated influenza vaccine for prevention of influenza in infants in Mali: a prospective, active-controlled, observer-blind, randomised phase 4 trial. Lancet Infect Dis doi:10.1016/S1473-3099(16)30054-8. doi:10.1016/S1473-3099(16)30054-8

[3]Ndungo et al., 2021. Repertoire of Naturally Acquired Maternal Antibodies Transferred to Infants for Protection Against Shigellosis. Front Immunol 12:725129. doi:10.3389/fimmu.2021.725129

Figure S3. Age-stratified distribution of mean tetanus toxoid IgG in children <2 years of age. Mean IgG antibody levels in infants and toddlers representing three age groups (6-8, 12-17, and 18-24 months) living in three regions: Afar (square) and Tigray (triangle), Ethiopia and Bamako (circle), Mali.
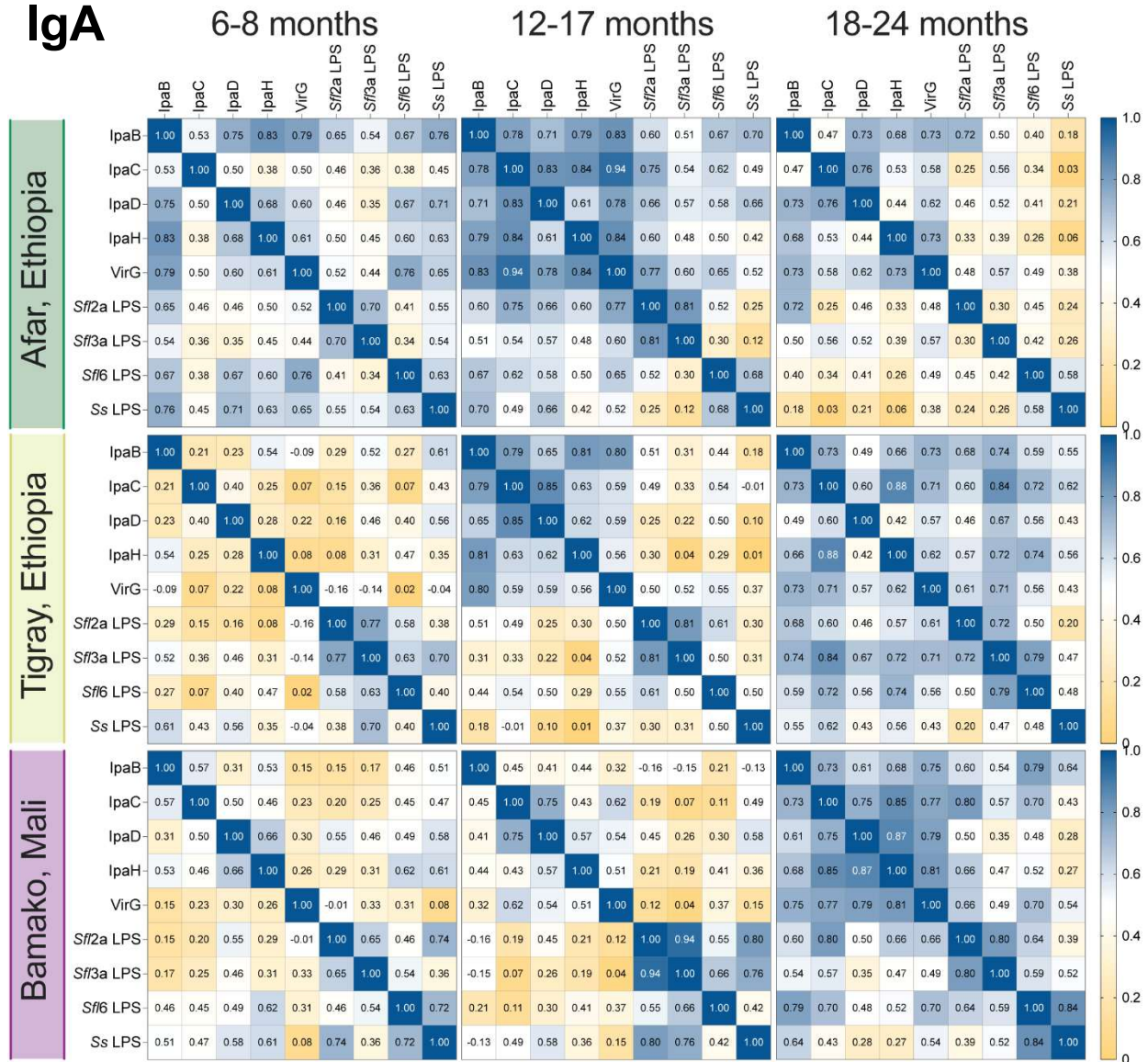
Figure S4. *Shigella* antigen-specific IgG correlations by age group and site. Heatmaps displaying correlations between antigen-specific IgG responses among children in Afar, Tigray, and Bamako. Spearman's correlation values are indicated in each cell.

Figure S5. *Shigella* **antigen-specific IgA correlations by age group and site.** Heatmaps displaying correlations between antigen-specific IgA responses among children in Afar, Tigray, and Bamako. Spearman's correlation values are indicated in each cell.