Annex 1

Research questions

There will be five research questions, one for each outcome evaluated:

1) **Sensitivity**: In persons newly diagnosed with TB disease (used as a proxy for diagnosis of TB infection), what is the diagnostic sensitivity of the index IGRA (TB-Feron, FIA, QIAreach, VIDAS, or T-Cell Select) compared to the reference IGRA (QFT-G, QFT-GIT, QFT-plus, T-Spot, or Wantai) or the TST?

2) **Specificity**: In persons at very low risk of TB infection (used as a proxy for individuals not infected with TB), what is the diagnostic specificity of the index IGRA compared to the reference IGRA or the TST?

3) **Inter-Test Agreement**: In persons tested for TB infection, what is the level of agreement between index IGRA and reference IGRA, or the TST (using Cohen’s Kappa statistic)?

4) **Intra-Test Reproducibility**: In persons tested for TB infection, what is the level of agreement of repeated testing performed on the same subject with the same tests (within-subject reproducibility) for the index IGRA?

5) **Predictive Ability**: In persons tested for TB infection and not treated, what is the ability of the index IGRA to predict future incidence of TB disease (minimum follow-up time of one year), relative to reference tests?