

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 IGRAs (TB-Feron, FIA, QIArearch, VIDAS, or T-Cell Select) compared to the reference IGRAs (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 IGRAs compared to the references IGRAs or the TST?
- 3) **Inter-Test Agreement:** In persons tested for TB infection, what is the level of agreement between index IGRAs and reference IGRAs, 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 IGRAs?
- 5) **Predictive Ability:** In persons tested for TB infection and not treated, what is the ability of the index IGRAs to predict future incidence of TB disease (minimum follow-up time of one year), relative to reference tests?