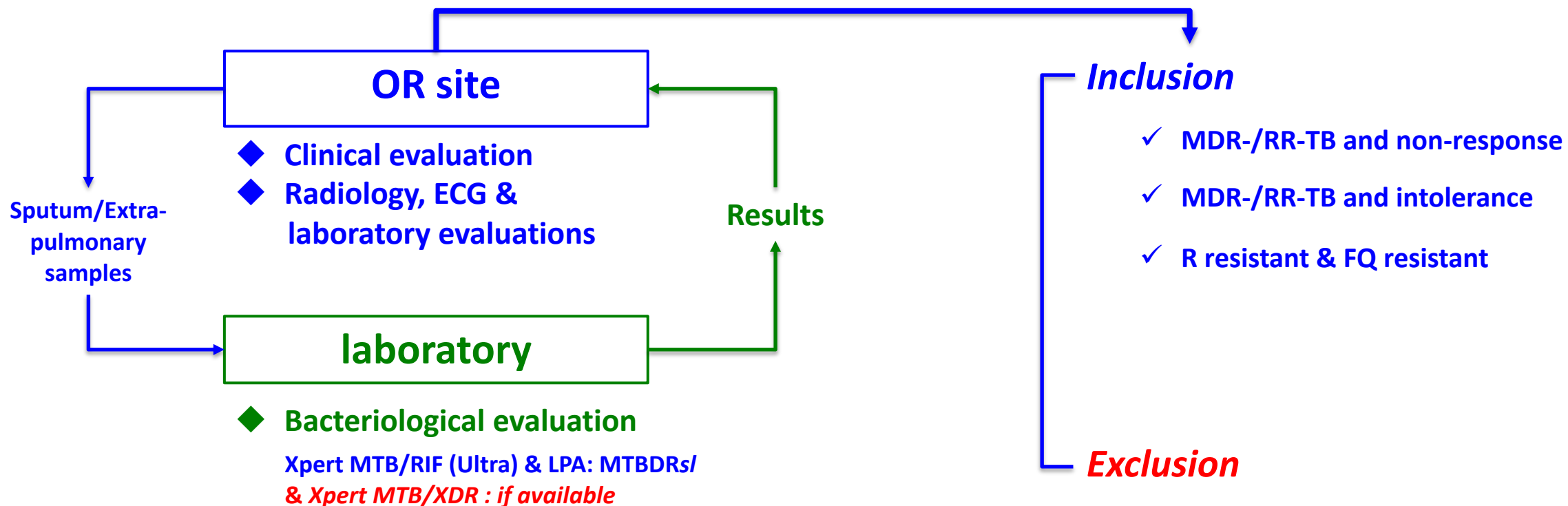
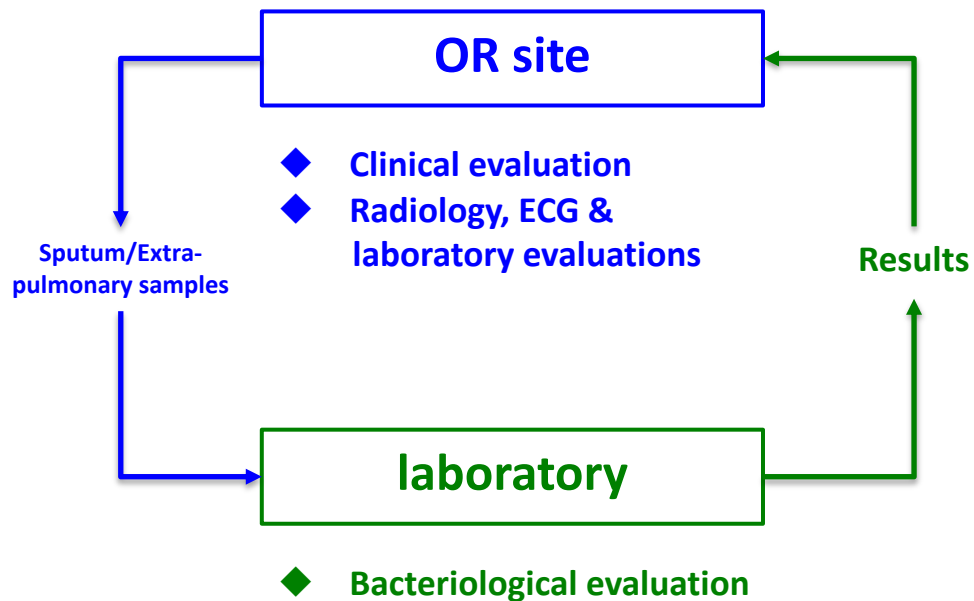


# *TOT Philippine: Bacteriological perspective*

## Patient inclusion: Bacteriological perspective



## Baseline examinations in the laboratory

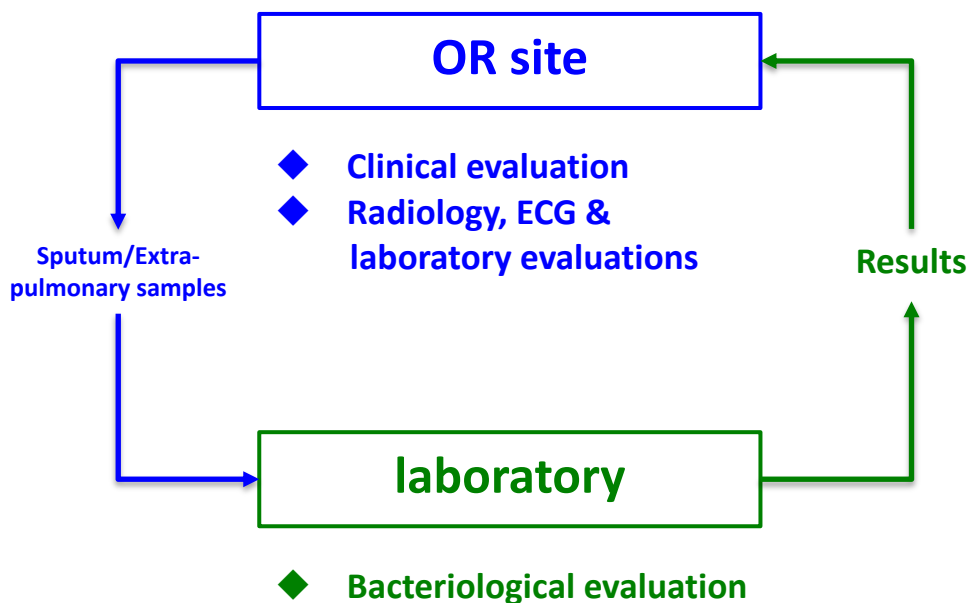


- Sputum smear
- Culture
- Sputum DST
  - Xpert MTB/RIF or Ultra
  - MTBDRs/
  - pDST for the second-line drugs

Isolates from positive cultures will be collected and stored for future research (pDST for BPaL, NGS, etc.).

## Examinations in monitoring evaluations

Monitoring will be done monthly, at the end of treatment, and at *6 and 12 months after treatment*



Extra-pulmonary samples (smear/culture/DST): if possible and no documented response to treatment

- Sputum smear
- Culture
- pDST if smear or culture positive
  - at month 4, end of treatment or post-treatment follow up
  - can be done once pDST for BPaL is available.

Isolates from positive cultures will be collected and stored for future research (pDST for BPaL, NGS etc.).

## New laboratory settings during LIFT-TB project

- Xpert MTB/XDR test platform
- pDST for the BPaL drugs: MGIT system

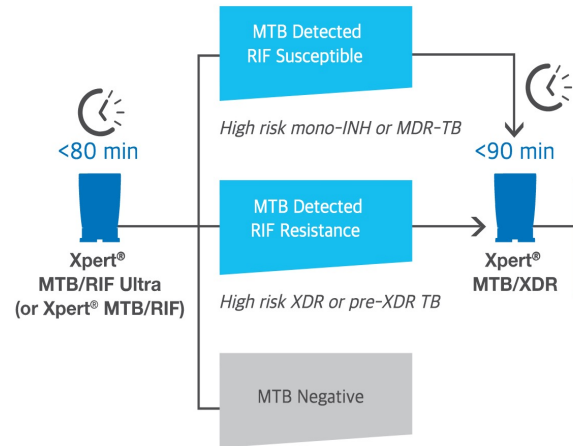
## Further research

Nest generation sequencing (NGS): Comparison of genotypes and resistance conferring mutations in case of relapse suspects

## Xpert MTB/XDR

Can detect :

INH / FQs / SLIDs / ETH



5 machines (new 10 color detection model) and 4,000 cartridges will be ready to go soon in the Philippine

**Even if XDR cartridge is available for the LIFT-TB project, do not replace LPA (MTBDRs/), but consider the Xpert XDR results as a reference: Even though WHO started to recommend to use Xpert XDR, accumulated clinical data up to now may not sufficient enough to replace MTBDRs/**

## Next generation sequencing

**Hopely there will be no BPaL regimen failure cases, but if there are some, expect identify resistant conferring mutations for pretomanid**

Table 6. Mutations associated with resistance to pretomanid in  $\geq 2$  isolates reported by  $\geq 2$  studies or  $\geq 3$  isolates reported by  $\geq 1$  study

Gene	aa change [nt]	MIC summary (relative to parent for available isolates)	MIC change by mutant/study	Data summary	References
<i>fbtC</i>	V720I [G2158A]	$\geq 1-10\times$	$\geq 10\times$ (1 isolate), $\geq 1\times$ (0.36 mg/L selection concentration, 3 isolates, parent MIC $\leq 0.36$ mg/L) $\geq 5\times$ (1.8 mg/L selection concentration, 1 isolate, parent MIC $\leq 0.36$ mg/L)	5 in vitro selected mutants, MIC testing done for only 1 isolate	Haver 2015 <sup>60</sup>
<i>fbtC</i>	P372S [C1114T]	$\geq 5\times$	$\geq 5\times$ (1.8 mg/L selection concentration, 3 isolates parent MIC $\leq 0.36$ mg/L)	3 in vitro selected mutants, MIC testing not performed	Haver 2015 <sup>60</sup>
<i>fbtC</i>	frameshift [ins C2549]	$\geq 5\times$	$\geq 5\times$ (1.8 mg/L selection concentration, 4 isolates, parent MIC $\leq 0.36$ mg/L)	4 in vitro selected mutants, MIC testing not performed	Haver 2015 <sup>60</sup>
<i>ddn</i>	S11*	$\geq 10\times$	$\geq 10\times$ (15 isolates)	15 in vitro selected mutants	Haver 2015 <sup>60</sup>
<i>ddn</i>	Y133D	$\geq 5\times$	$\geq 5\times$ (1.8 mg/L selection concentration, 3 isolates)	3 in vitro selected mutants, MIC testing not performed	Haver 2015 <sup>60</sup>

**THANK YOU**

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FOR QUESTIONS AND INQUIRIES**

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