

DISCORDANT RESULTS IN DRUG SUSCEPTIBILITY TESTING: A clinician's experience

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Discordance



- **“A state of non-harmony or non-agreement”**
- **Non-agreement between**
 - **Different genotypic tests**
 - **Genotypic and phenotypic tests**
 - **1 or more of genotypic and/or phenotypic tests and clinical response to treatment**



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Diagnostic Tests



XPERT/MTB RIF (GeneXpert) – initial diagnostic test

Line Probe Assay (MTBDRplus) – confirmatory test

Both Genotypic tests



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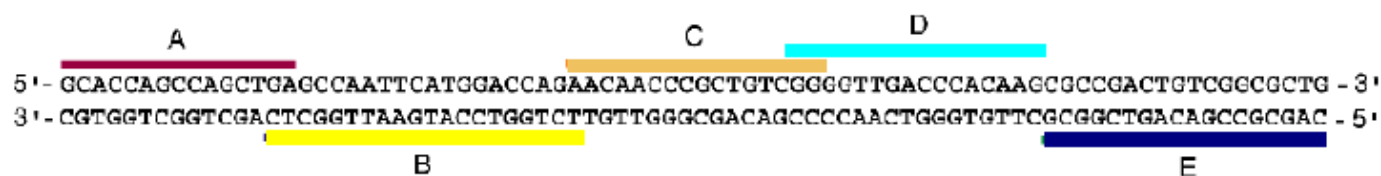
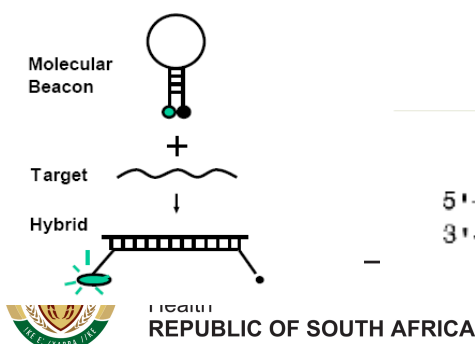
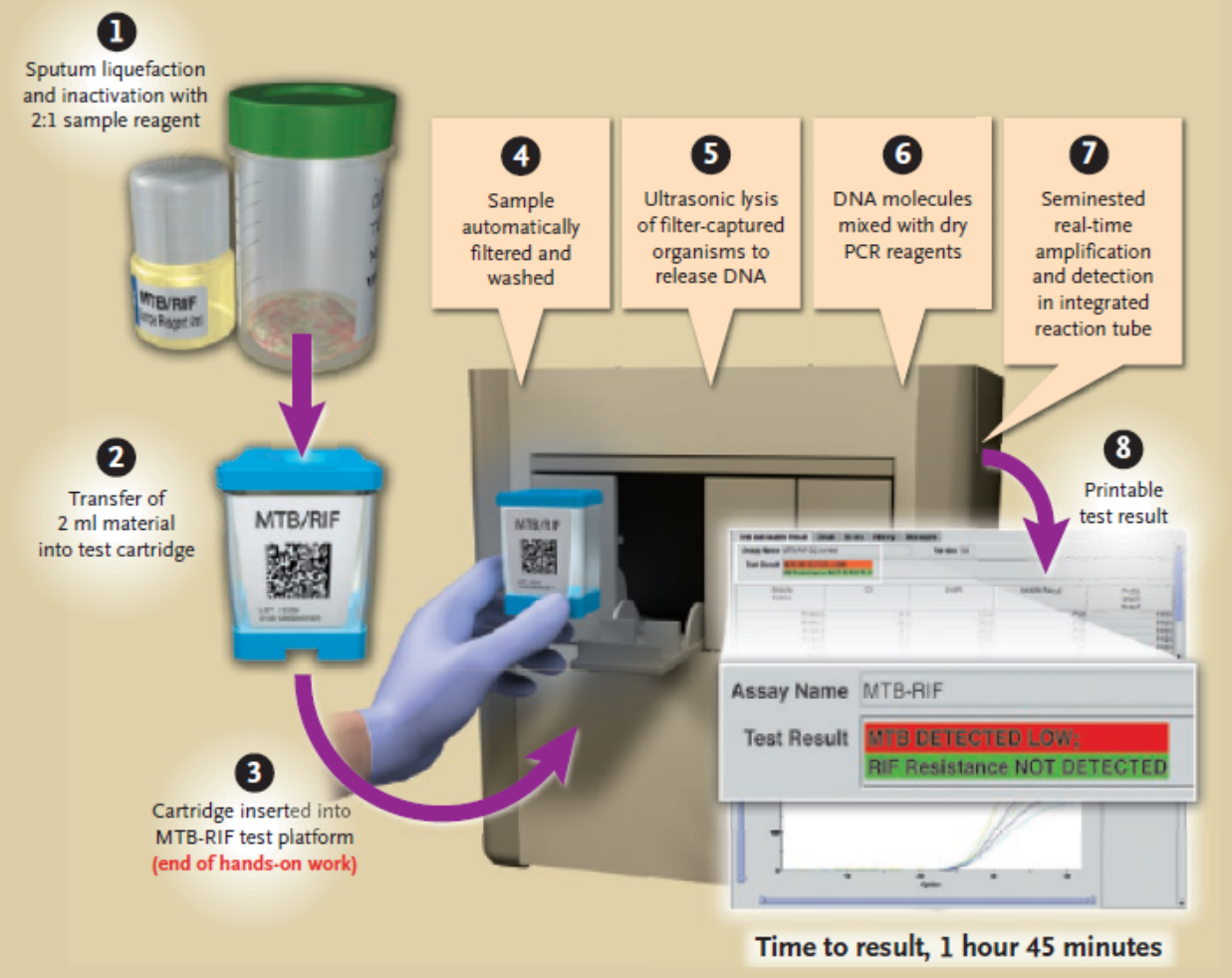


Boehme, C et al NEJM 2010

Gene Xpert MTB/RIF:

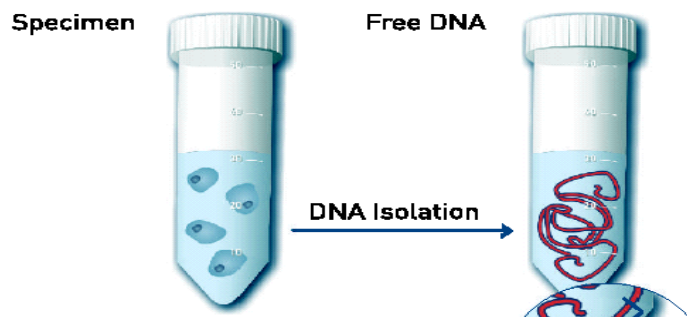
Total processing
time = 2 hours
Reportable
result:

- Positive/negative TB
- Resistance yes/no to Rifampicin





1 DNA Extraction



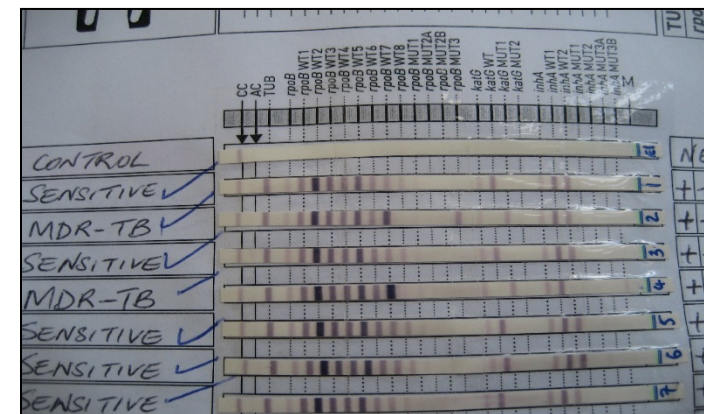
2 Amplification (PCR)



3 Hybridization (Detection)



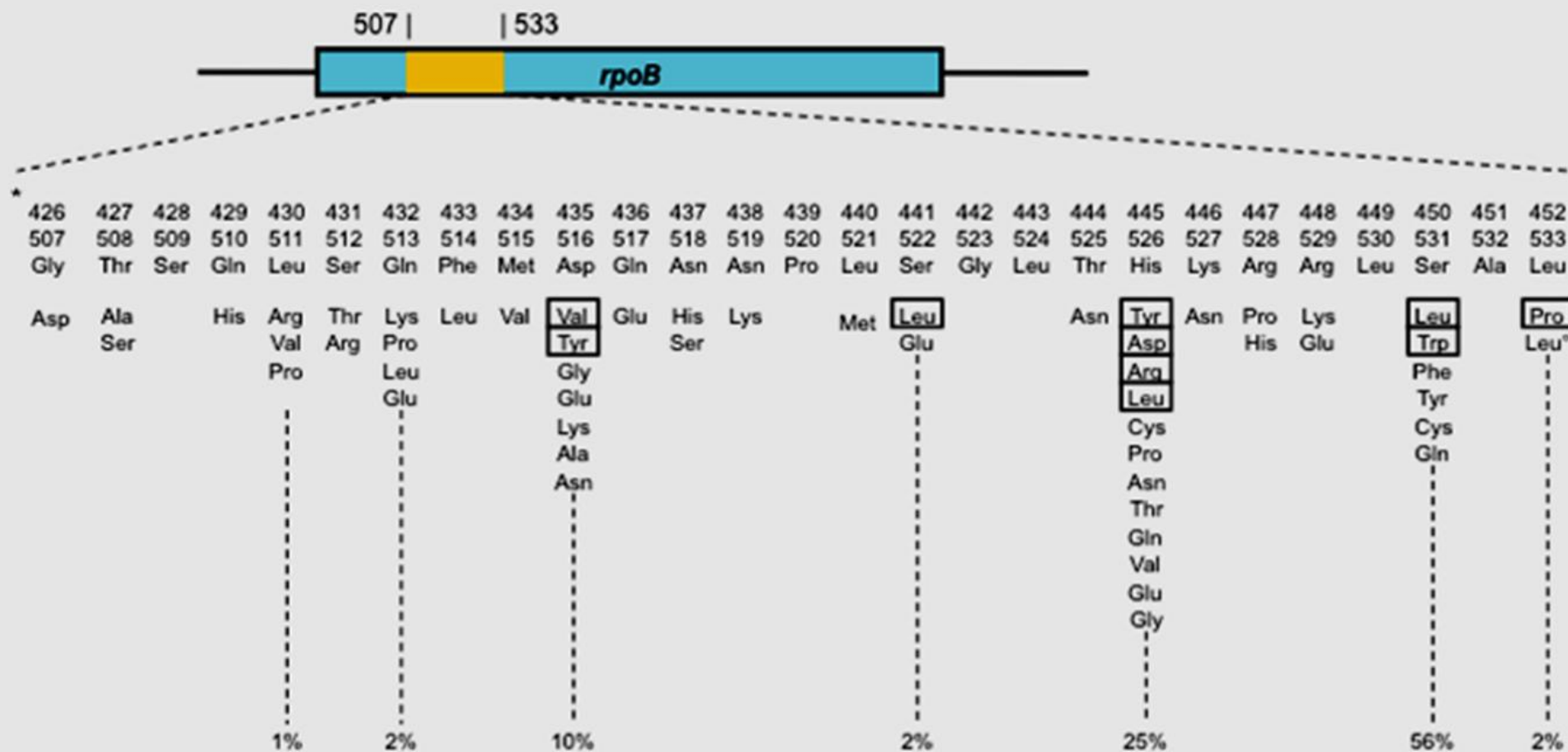
4 Result interpretation



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* *M. tuberculosis rpoB* gene
Codons are numbered according to the *rpoB* gene of *Escherichia Coli*



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Case Scenario 1



Ms. S.F

30 year old female

HIV Neg

No previous TB episode

Significantly ill, weak, emaciated at baseline

BMI – 15kg/m²

Requiring admission

GeneXpert = RR

LPA = SS



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Case Scenario 2



Mr. D.M

48 year old male

HIV Pos – defaulted ART

CD4 86, CLAT - Neg

No previous TB episode

Clinically Stable at baseline

Not Requiring admission

GeneXpert = RR

LPA = SS



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What does this mean??

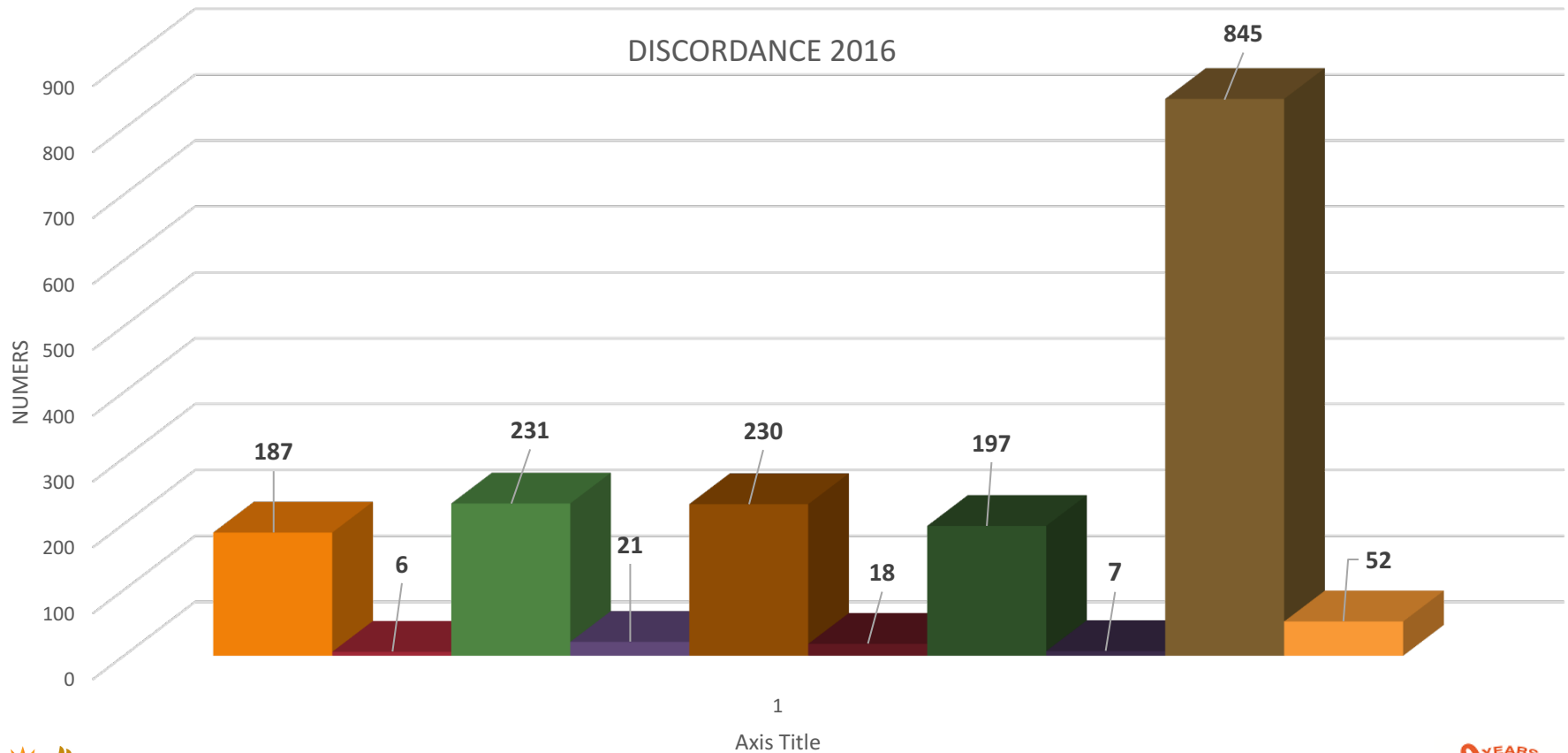
What do we do about it??



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Discordant Results 2016

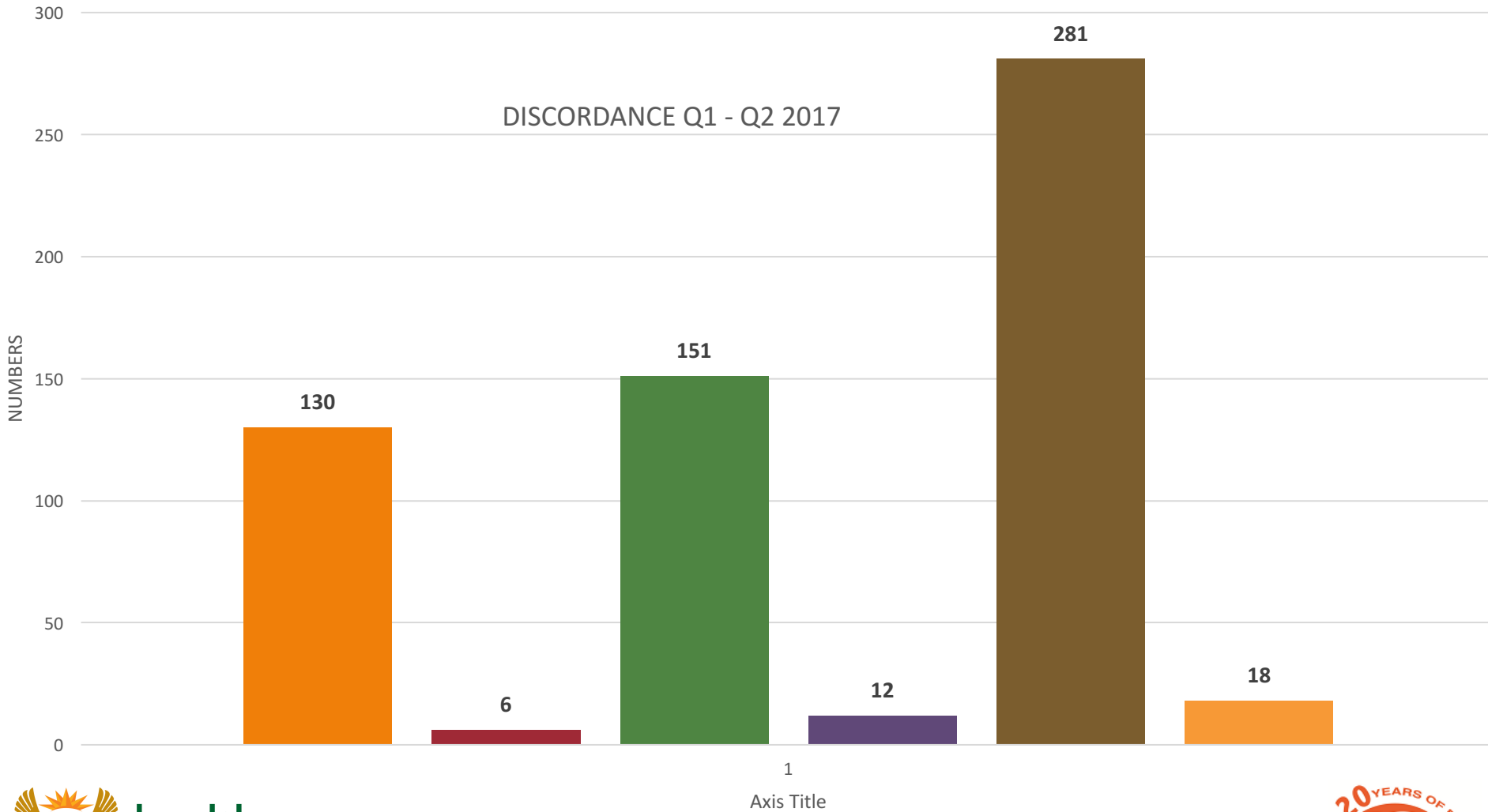


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Discordant Results 2017



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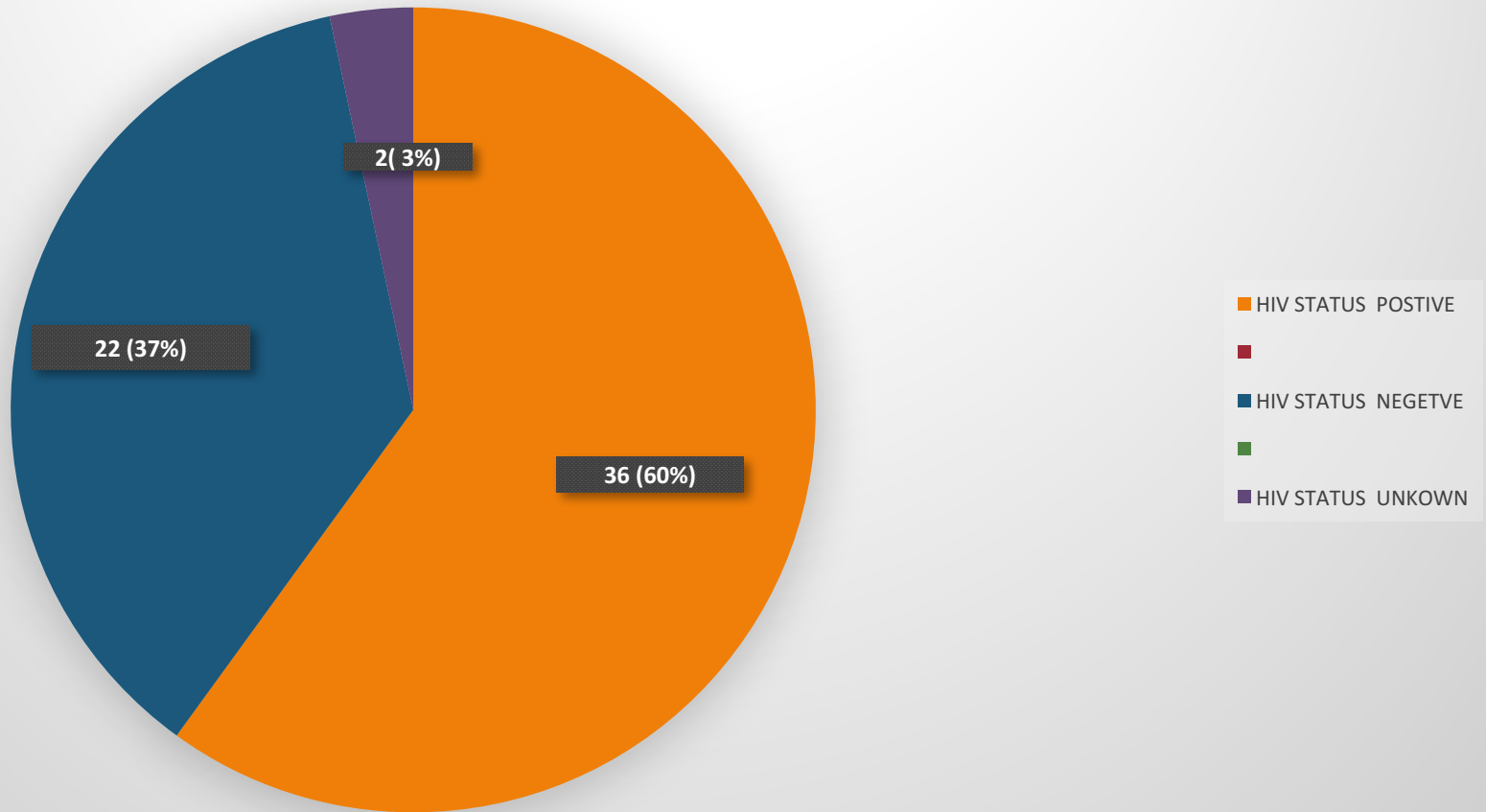
Q1 TOTA MDR Q1 DISCORDANT Q2 TOTA MDR Q2 DISCORDANT TOTAL DISCORDANT



HIV Status



HIV STATUS



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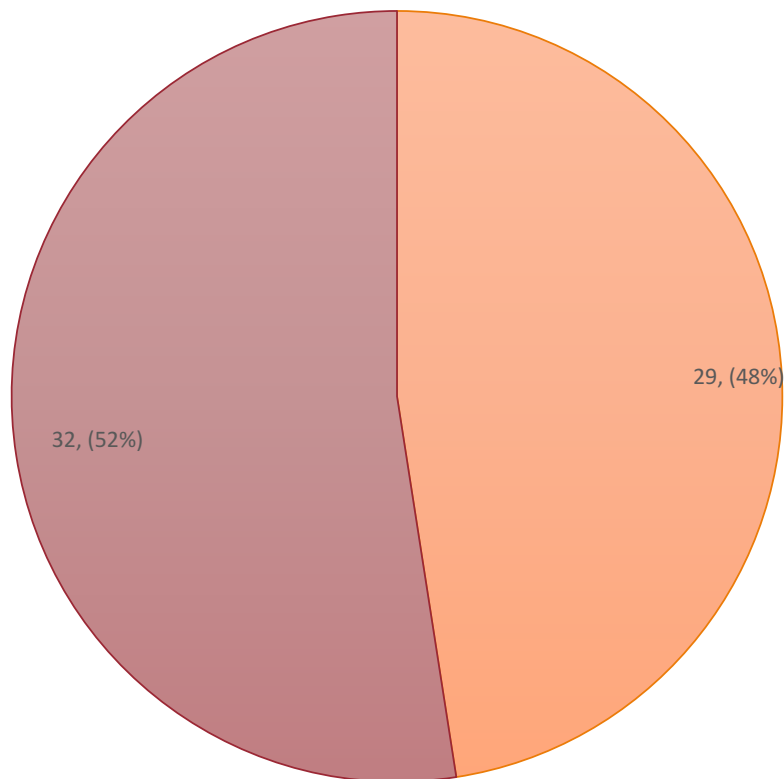
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Gender



GENDER



■ GENDER MALE ■ GENDER FEMALE

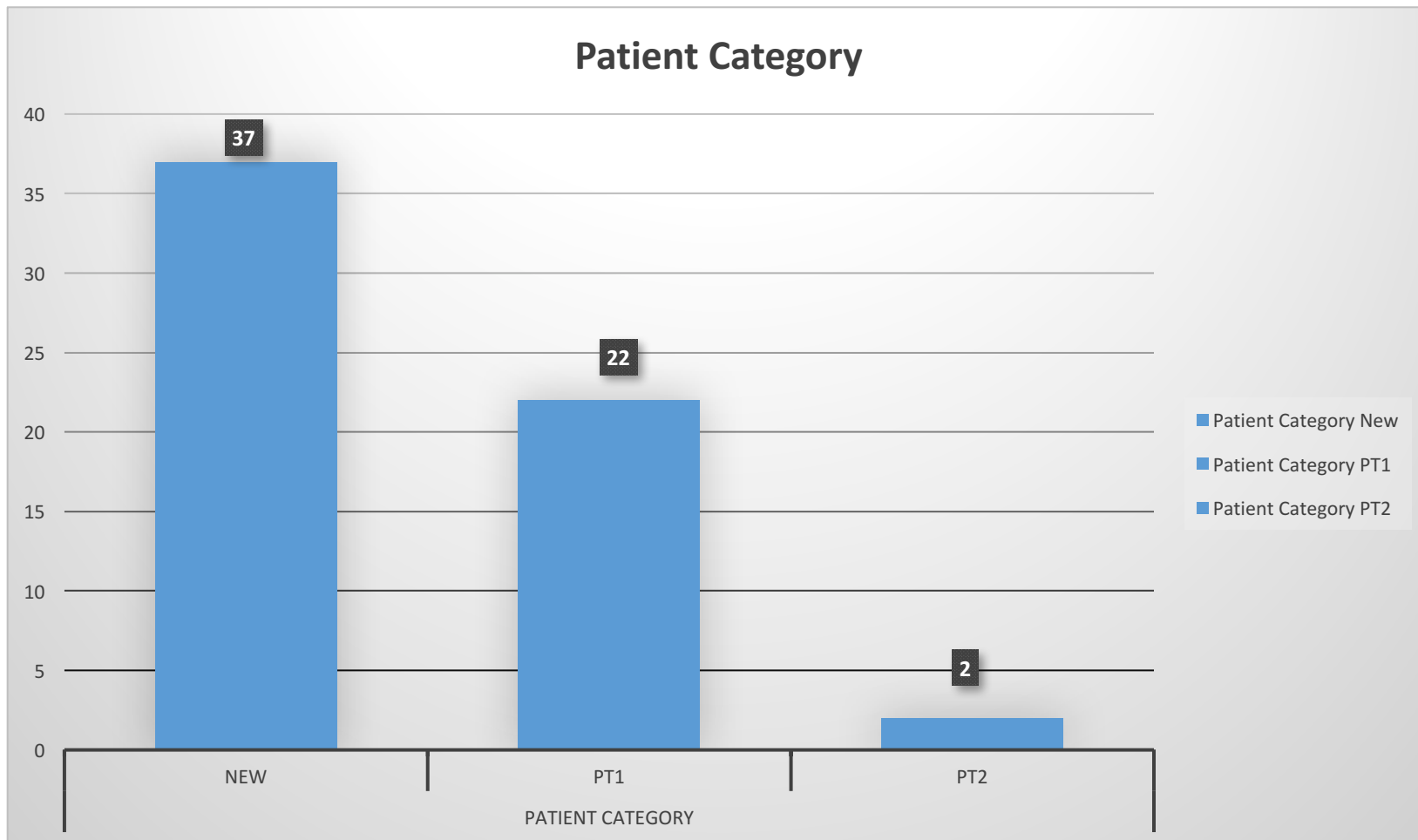


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Patient Category



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Course of Action



- 1. Standard MDR TB treatment continued**
- 2. Rifampicin and INH added to the MDR regimen**
- 3. MDR treatment stopped and patient treated with RHZE (standard Regimen 1 or RHZE for full duration of treatment)**



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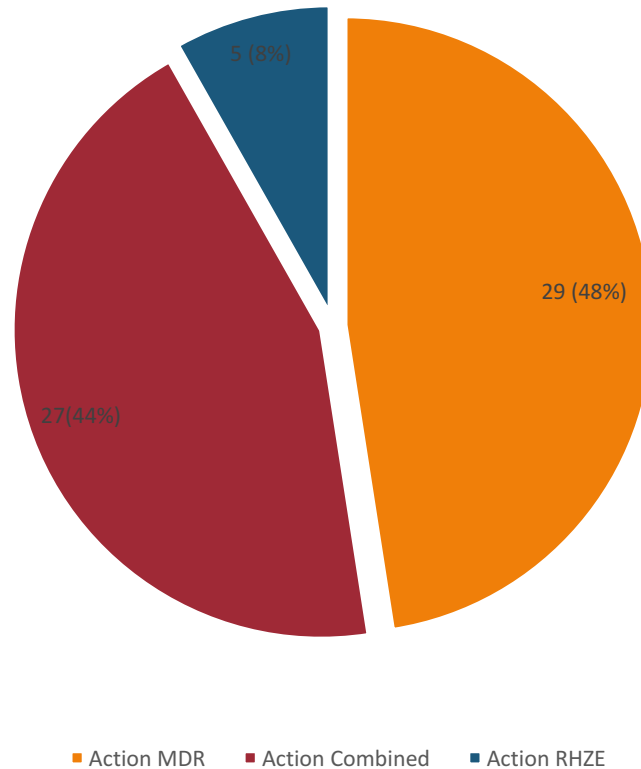
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Course of Action



Action



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Major Determinants of Course of Action



1. Patient Category :

**All patients with previous TB treatment episode
...were continued on their MDR treatment (RiF &
INH added for 9/24 patients)**

2. Clinical Condition at Baseline

**Clinically well patients had a higher probability of
having MDR treatment stopped**



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Treatment Outcomes



CURED = 4 (RHZE patients)

LTFU = 5 patients

DIED = 5 patients = (all on MDR treatment +/- RH)

STILL ON TREATMENT = 51/61 patients are stable and well on course towards treatment completion



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Observations



Majority of the discordant samples – Smear Negative (56/61)

Most (57/61) patients culture converted in Month 1 or 2 (paucibacillary disease) – irrespective of course of action taken



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Challenges



- **Patient counseling and explanation of Discordant Results**
In-patient issues where do you admit the patient – MDR vs DS TB ward

Very few PHENOTYPIC DST done - were culture Negative by the time DST was requested.

Confusing lab results – LPA SS but same specimen is Culture Negative

Adverse Drug Reactions >>> Drug-drug Interactions e.g Bedaquiline and Rifampicin



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Problems:

Genotype-phenotype relationship is not clearly understood

Geographic variability in distribution of mutations

Heteroresistance and mixed infections

Not all genetic mechanisms for resistance are

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Conclusion



Development in diagnostics – greatly reduced time to treatment initiation

New challenges brought to light – discordance between the genotypic tests and even genotypic-phenotypic

GOLD STANDARD ??

PRACTICALLY on the ground – shorter regimen has reduced our anxiety about discordant patient management



Acknowledgements



Nkqubela TB HOSPITAL

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UCT**

SAMRC

Eastern Cape TB Directorate



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