



Laboratory Analysis for Drug Assurance

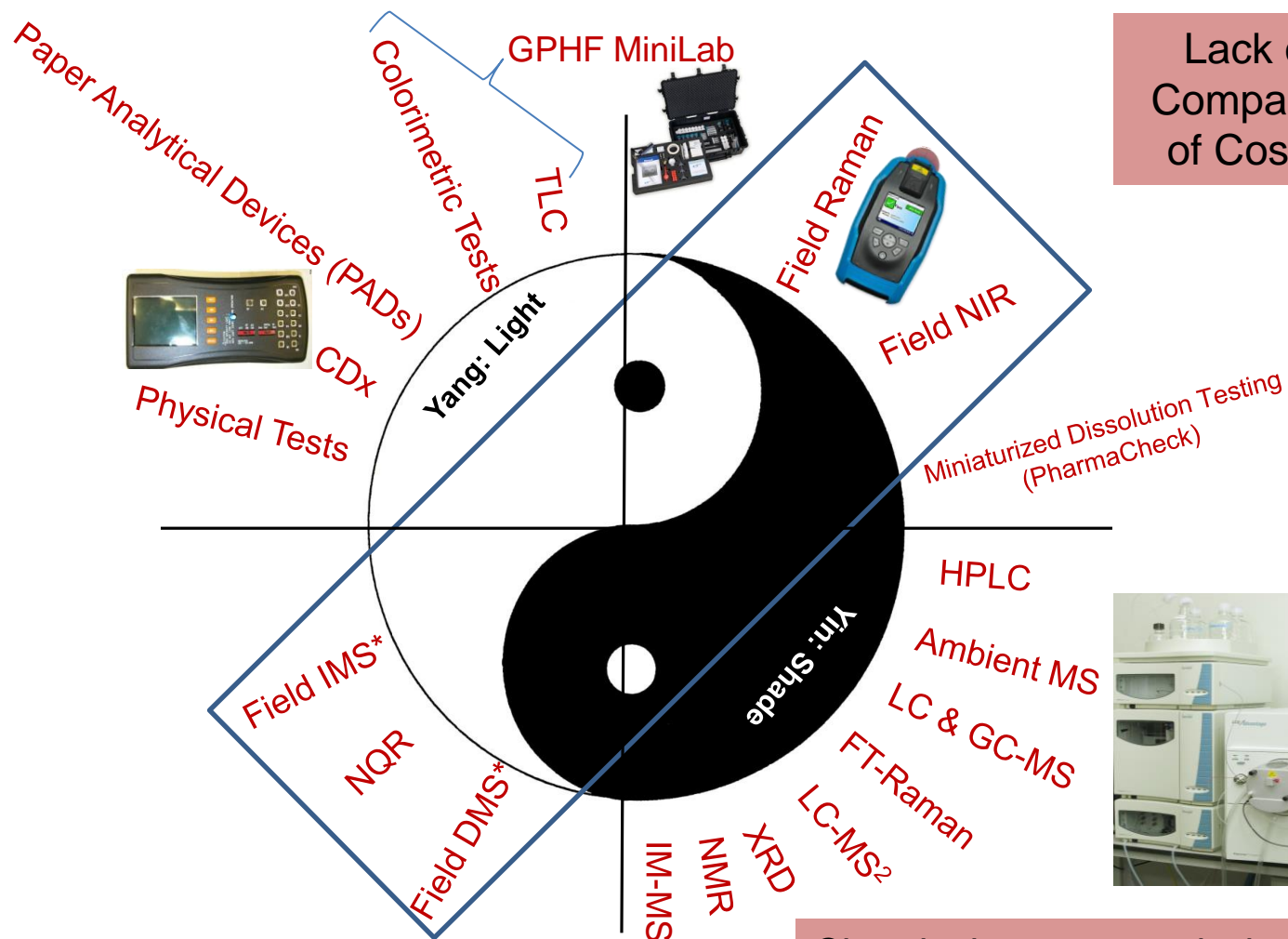
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¹London School of Hygiene & Tropical Medicine, ²Centre for Disease Control and Prevention, ³Georgia Institute of Technology



The Yin & Yang of Chemical Detection Technologies

A Chinese concept describing how seemingly opposite concepts interrelate to one another.



Lack of Systematic Comparisons in Terms of Cost/Performance



Chemical content analysis – “Gold Standard”

Laboratory Techniques available at LSHTM

Test 1



Test 2



- Colorimetric Screening Test

- HPLC



- Dissolution Testing



- LCMS



Artemisinin Derivatives Screening Tests



Tablet of
artemether/lumefantrine



Pulverise



Solution in
methanol

Presence of artemisinin derivative in tablet results:

- pink colour with the reagent DNP
- a Prussian blue colour with FBS

Spot solution on
matrix →

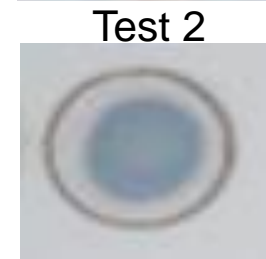


DNP →

Add reagents



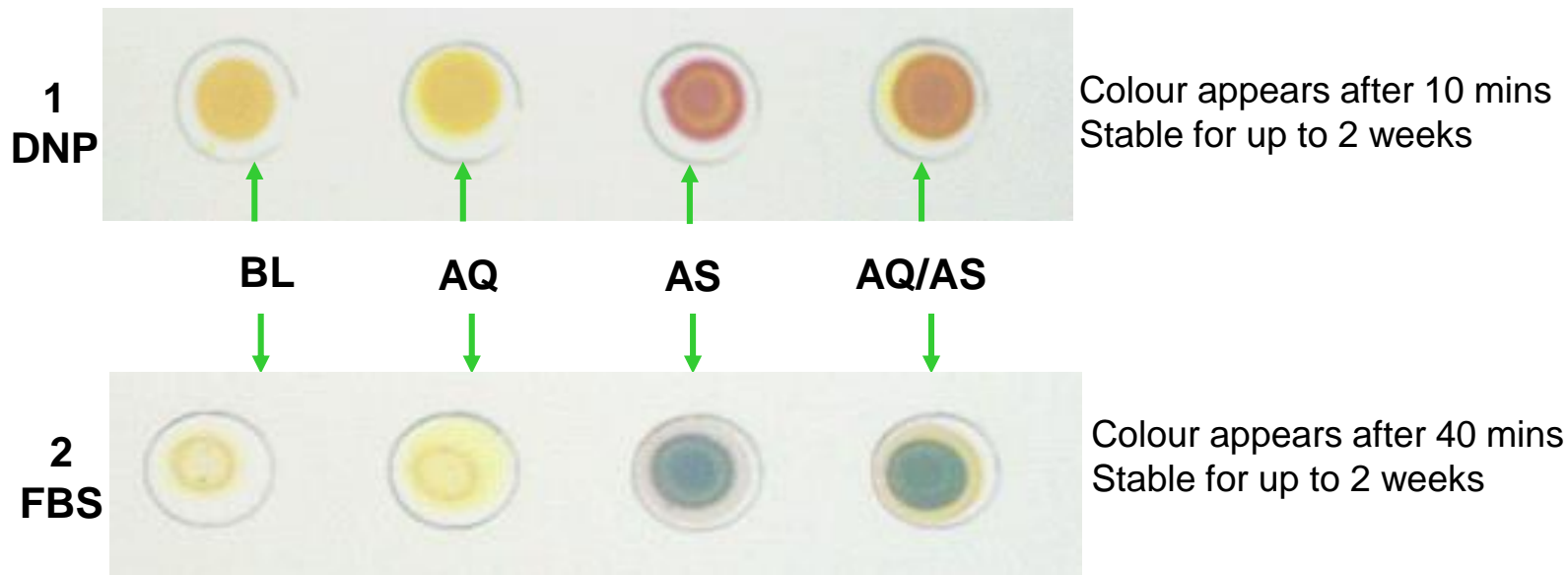
FBS →



Positive tests confirms presence
of artemisinin derivative

Colour Change Reaction on TLC for the Specific Detection of Artemisinin component

TWO assays



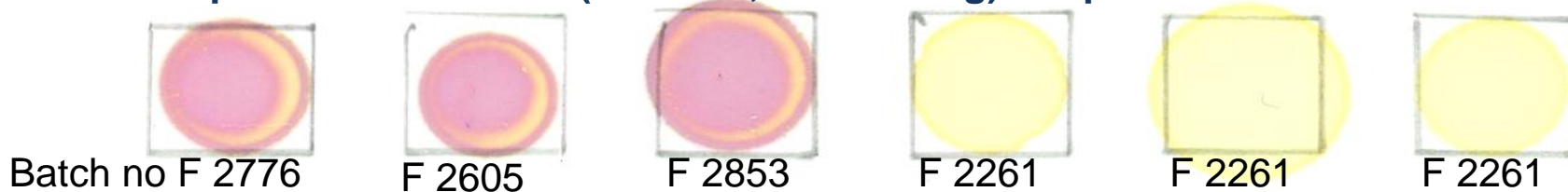
BL = Methanol

AQ = Amodiaquine

AS = Artesunate

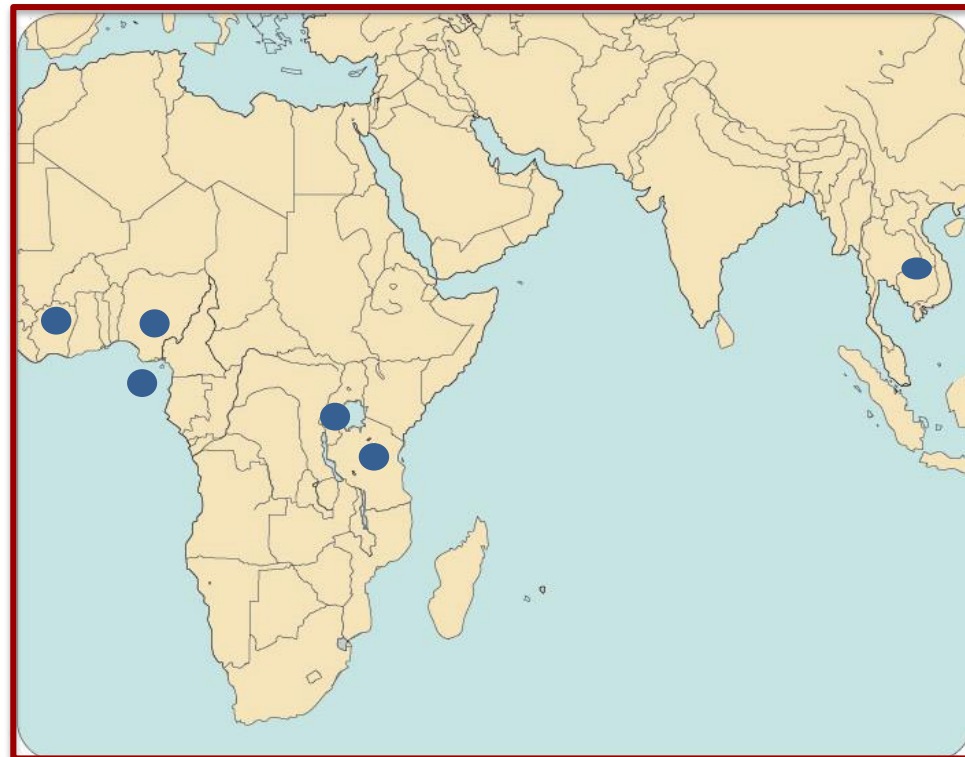
AS/AQ = Combination tablet (50 /150 mg) from Ghana

Samples of Coartem 24 (AM/LUM, 20 / 120 mg) – report in Wall St Journal



Methods used for the ACTc funded work

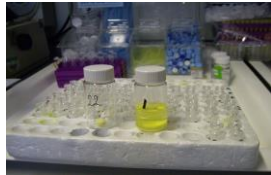
Chemical content analysis of >10,000 samples, 142 brands, from 6 countries



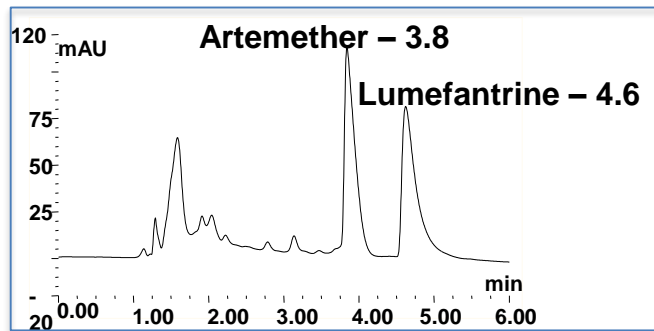
Chemical Content Analysis of ACTs



% Active ingredients



HPLC

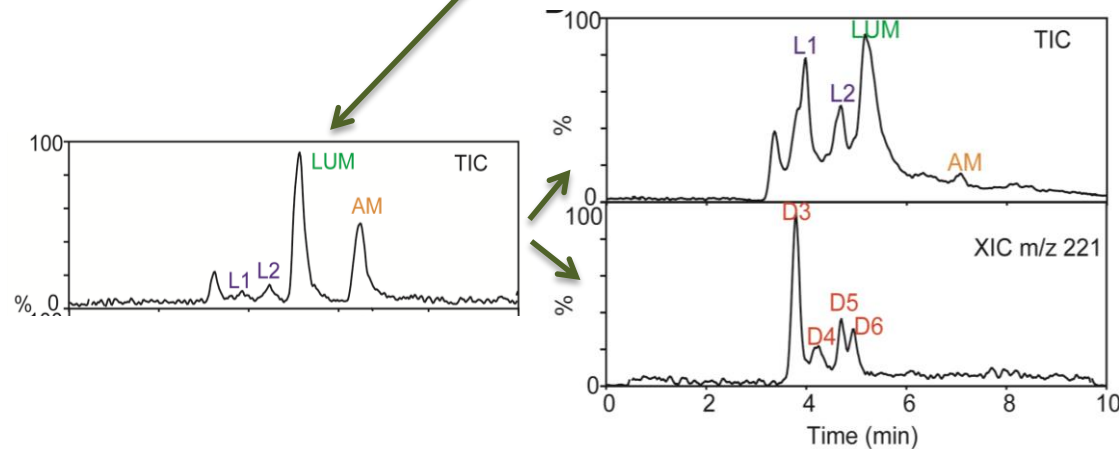


Degradation studies

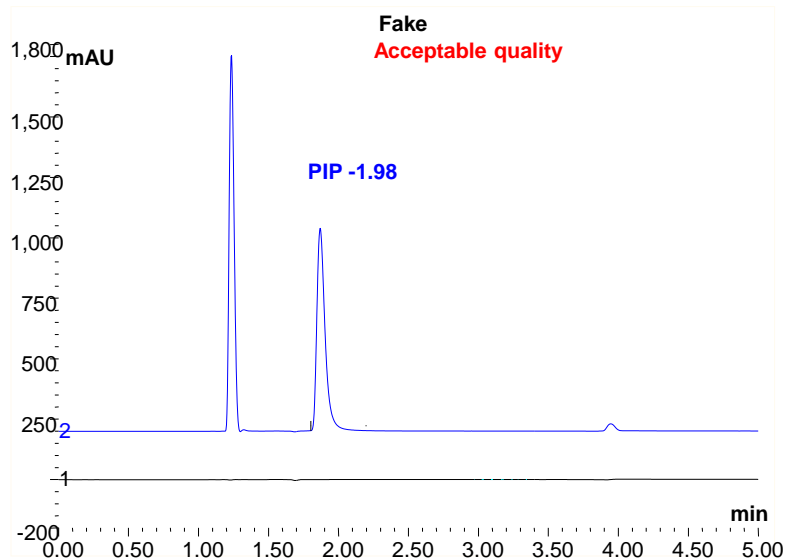
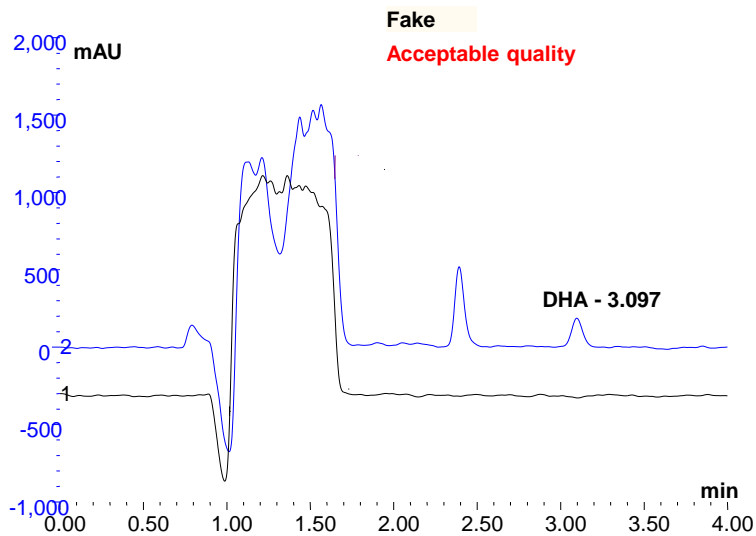
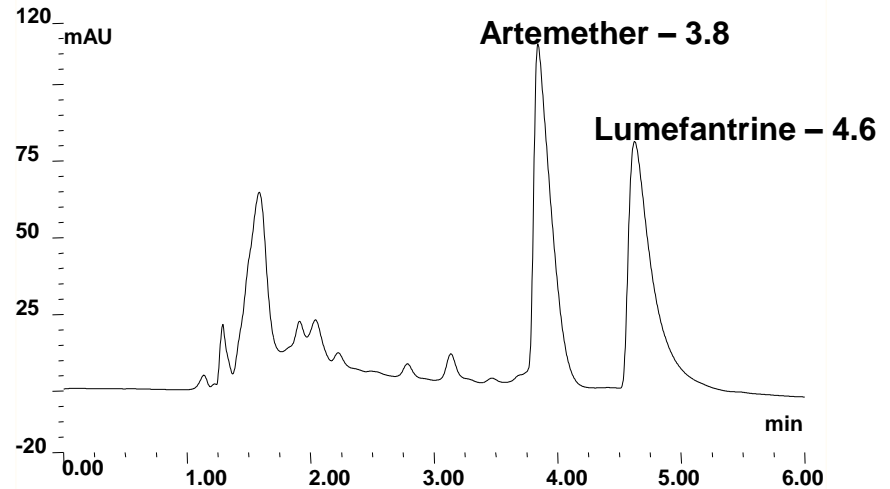
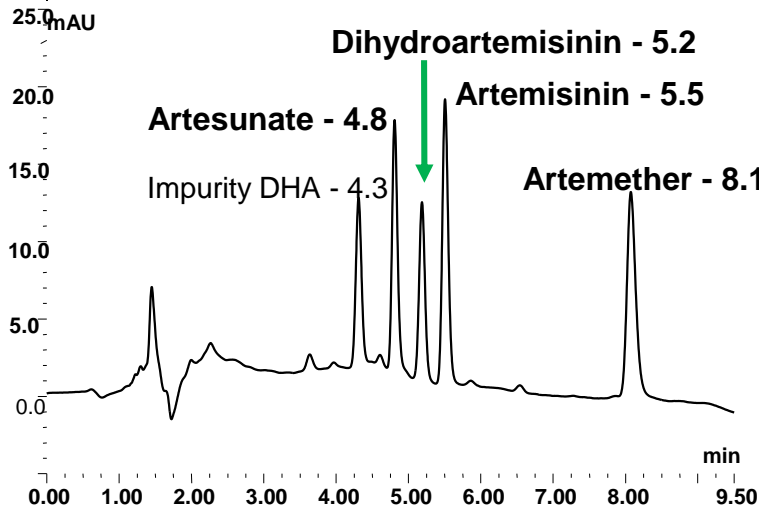


Forced ageing at 60°C
0 - 21 days

LC/MS



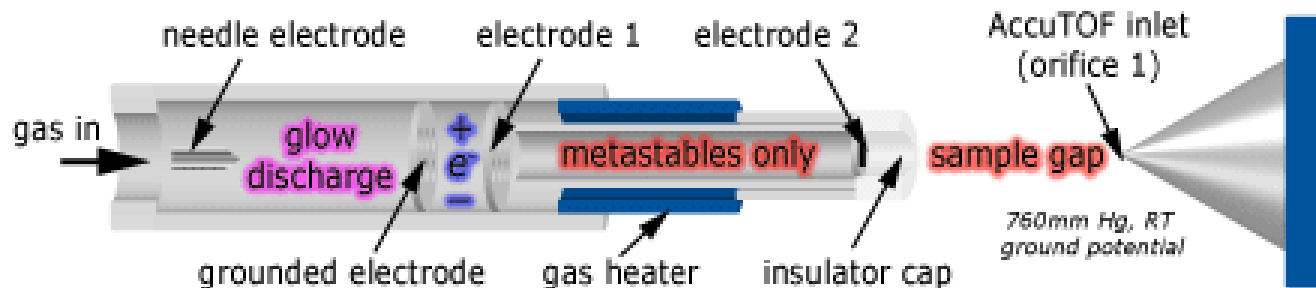
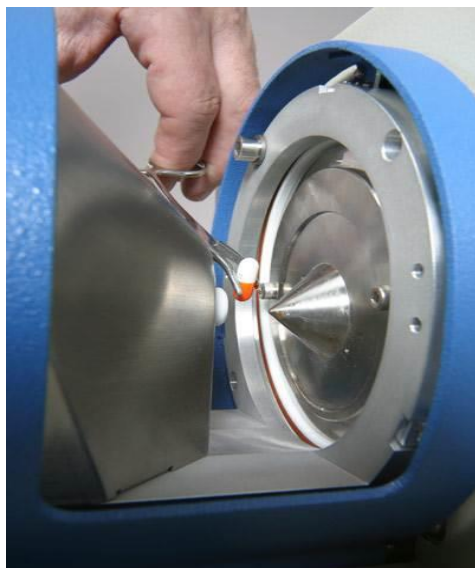
HPLC analysis at LSHTM & CDC



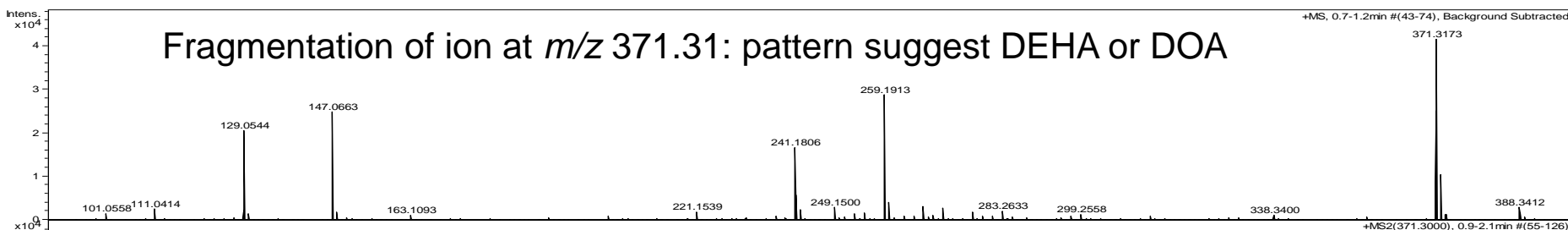
Classification of ACTs

| Drug quality | % Stated API detected | Method used |
|---------------------|------------------------------------|--------------------|
| Acceptable quality | 85-115 | HPLC & MS & LC/MS |
| Falsified | 0 | HPLC & MS & LC/MS |
| Substandard | < 85 - > 115 | HPLC & MS & LC/MS |
| Degraded | < 85 plus products of degraded API | MS & LC/MS |

The Yang: DART-MS AT Georgia Tech



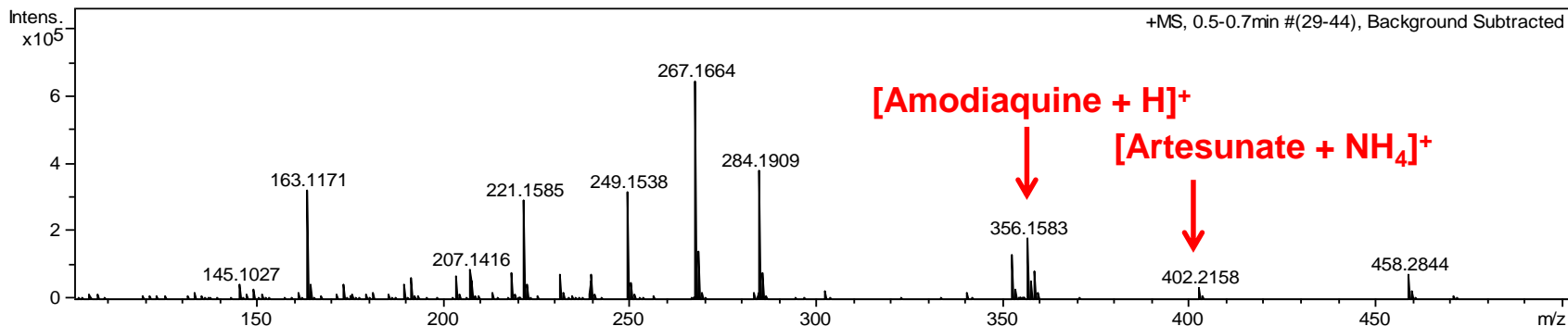
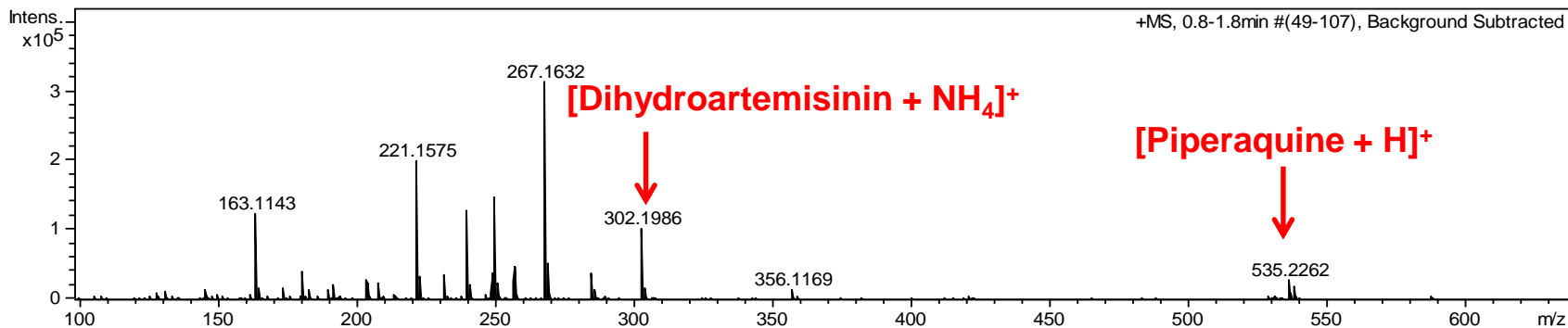
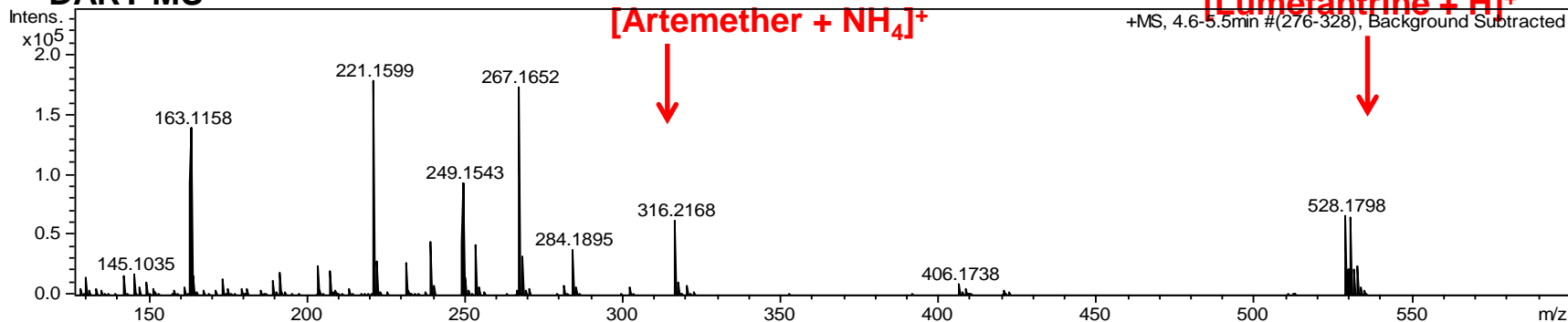
Fragmentation of ion at m/z 371.31: pattern suggest DEHA or DOA



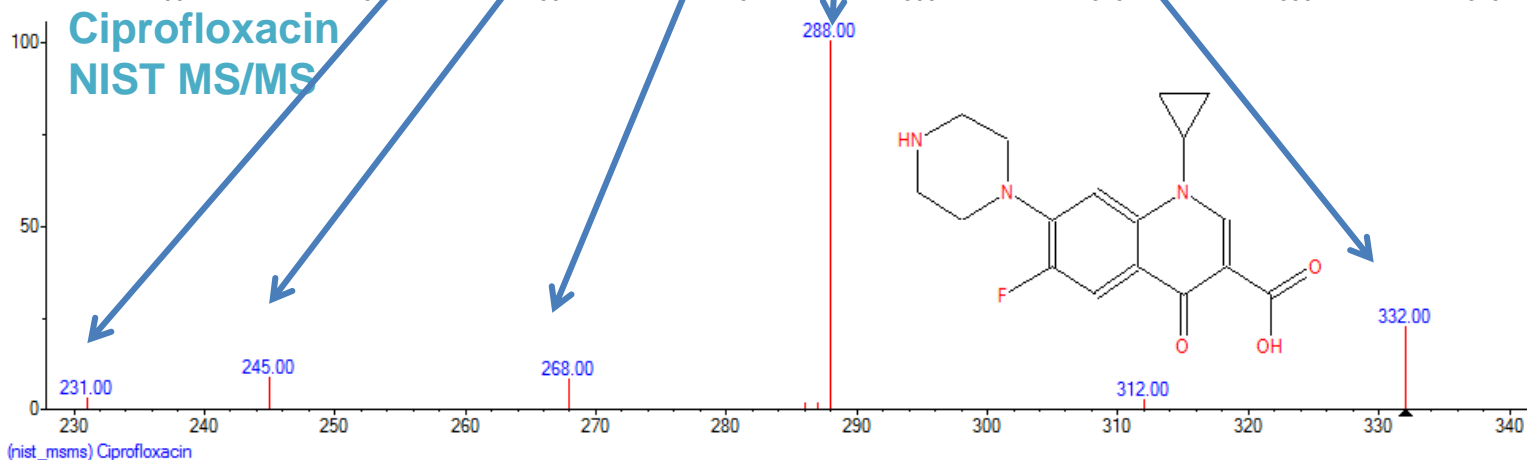
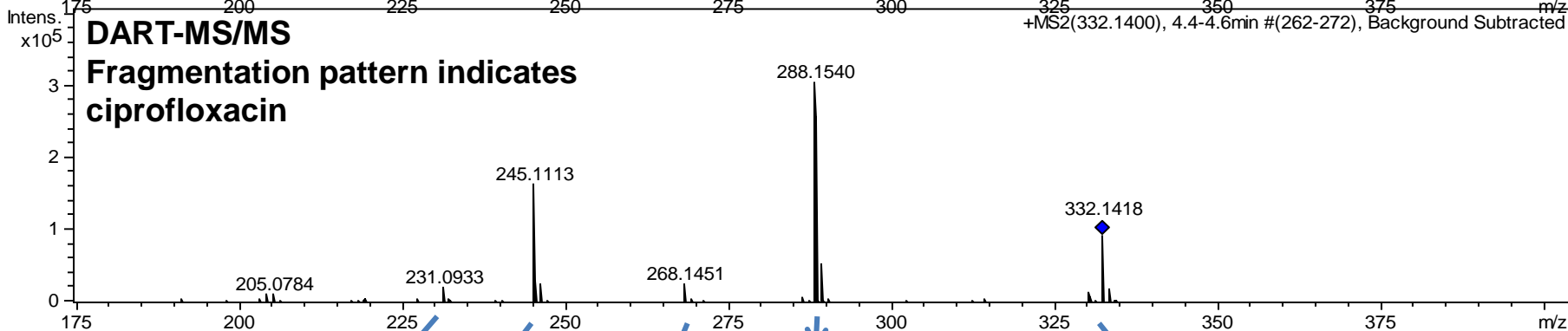
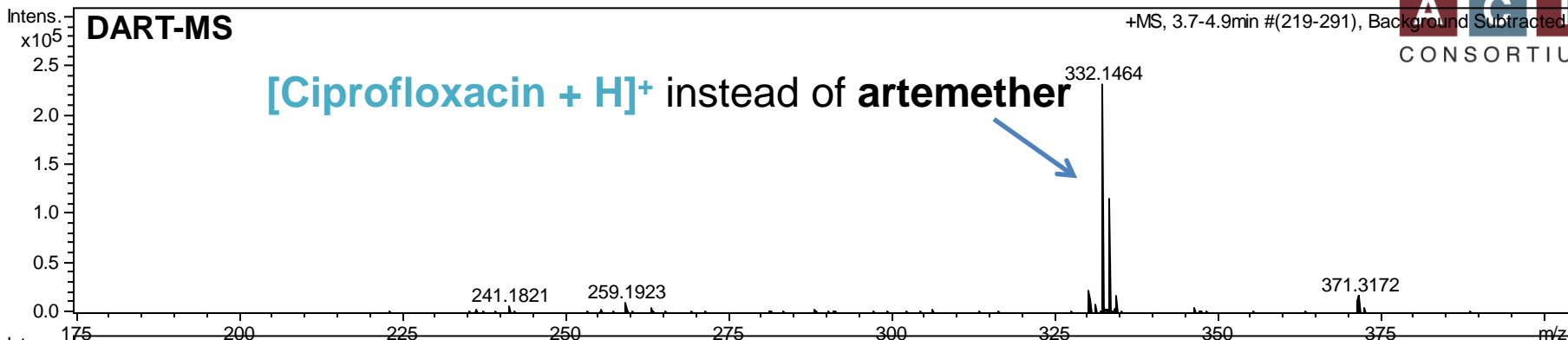
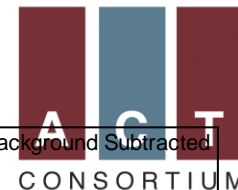
Nigeria ACT Results: Samples of Acceptable Quality



DART-MS



Nigeria ACT Results: Falsified samples



(nist_msms) Ciprofloxacin

ACKNOWLEDGEMENTS

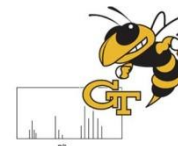
ACTc – DQ teams at LSHTM, CDC and GT

- A van Wyk, L Allan, Z Hall, N Malik, J Long, P Dwivedi, M J Culzoni, I Swamidoss, D Hostetler

Masters students - M El Sherbiny, I Fadeyi & I Mamadu

Teams on the ground purchasing and packaging the samples

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More information

www.actconsortium.org/drugquality

<http://malaria.lshtm.ac.uk/facilities/analytical-service-measuring-antimalarials-drugs-and-insecticides>

