

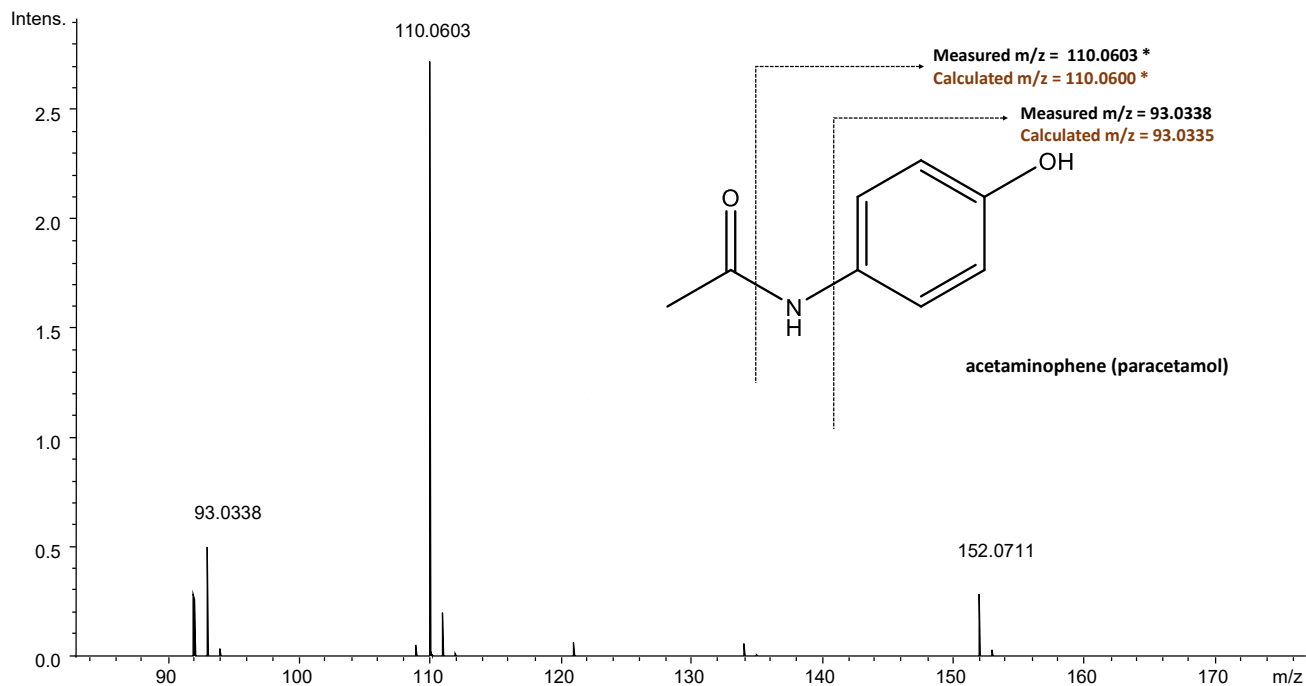
Supplementary PDF I:

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Figure S1: HR - MS/MS Fragmentation pattern measured for the falsified penicillin V tablets QMCA035

HR - MS/MS Fragmentation pattern measured from the falsified penicillin V samples (QMCA035) collected in the Republic of Cameroon, actually containing acetaminophen (paracetamol) The exact m/z of the paracetamol parent ion measured was 152.0711 (calculated 152.0706).



*the fragment ion with a m/z of 110, results from the protonated 4-aminophenol ($[H_2N-C_6H_4OH+H]^+$) formed by loss of ethone ($H_2C=C=O$).

Figure S2: HR - MS/MS Fragmentation pattern measured for the falsified metronidazole tablets QMC266

HR - MS/MS Fragmentation pattern measured from the falsified metronidazole tablets (QMC266) collected in the DR Congo, actually containing metronidazole benzoate.

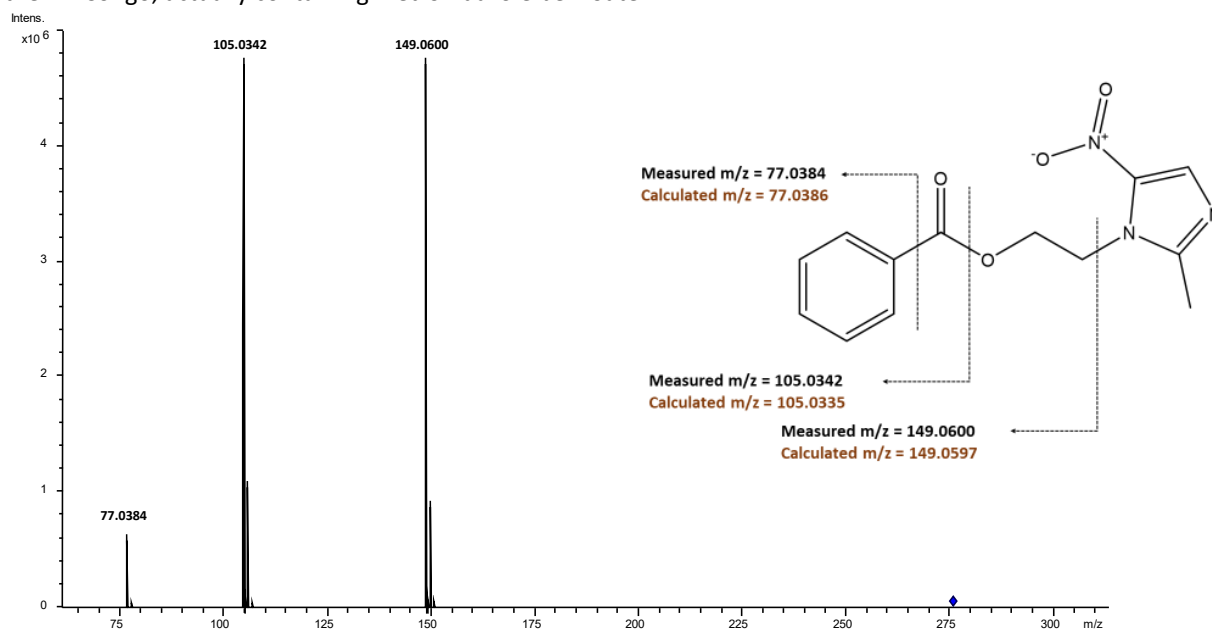


Figure S3: ^1H NMR spectrum (400 MHz, d_4 -MeOH) of the sample QMC266

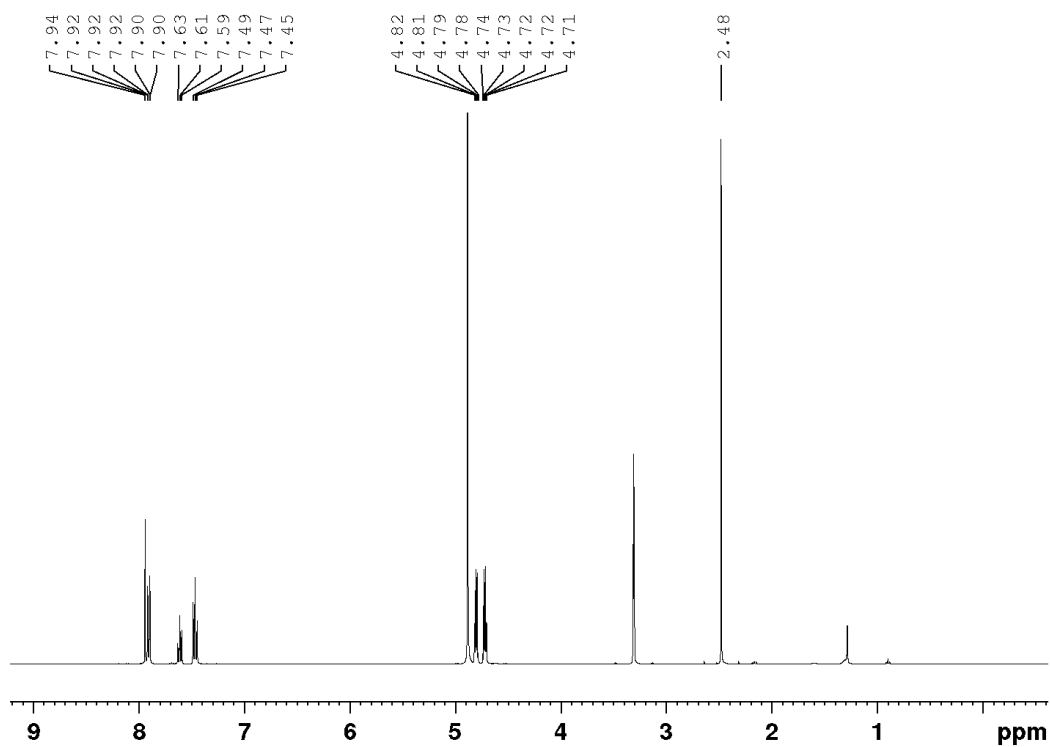


Figure S4: ^{13}C NMR spectrum (101 MHz, d_4 -MeOH) of the sample QMC266

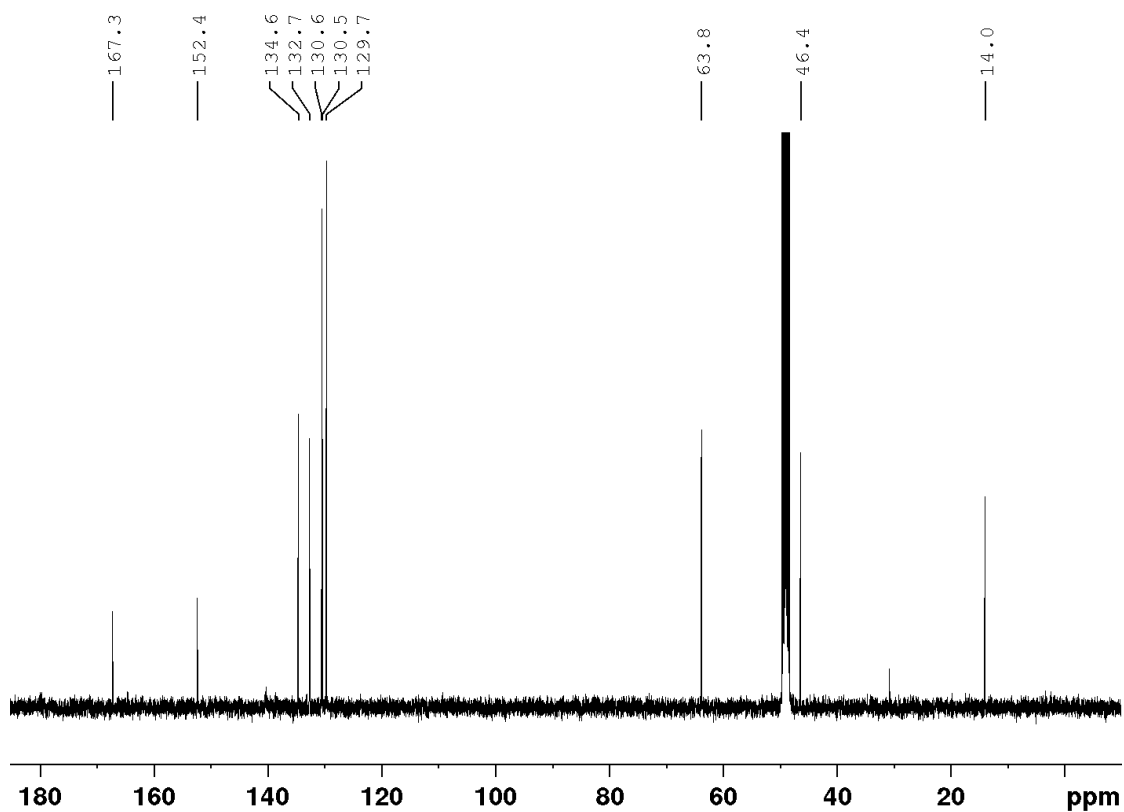


Figure S5: Edited ^1H - ^{13}C HSQC NMR spectrum (400 MHz, d_4 -MeOH) of the sample QMC266

This experiment reveals which proton is directly bond to which carbon. Blue cross peaks indicate CH and CH_3 moieties, while red cross-peaks indicate CH_2 -groups.

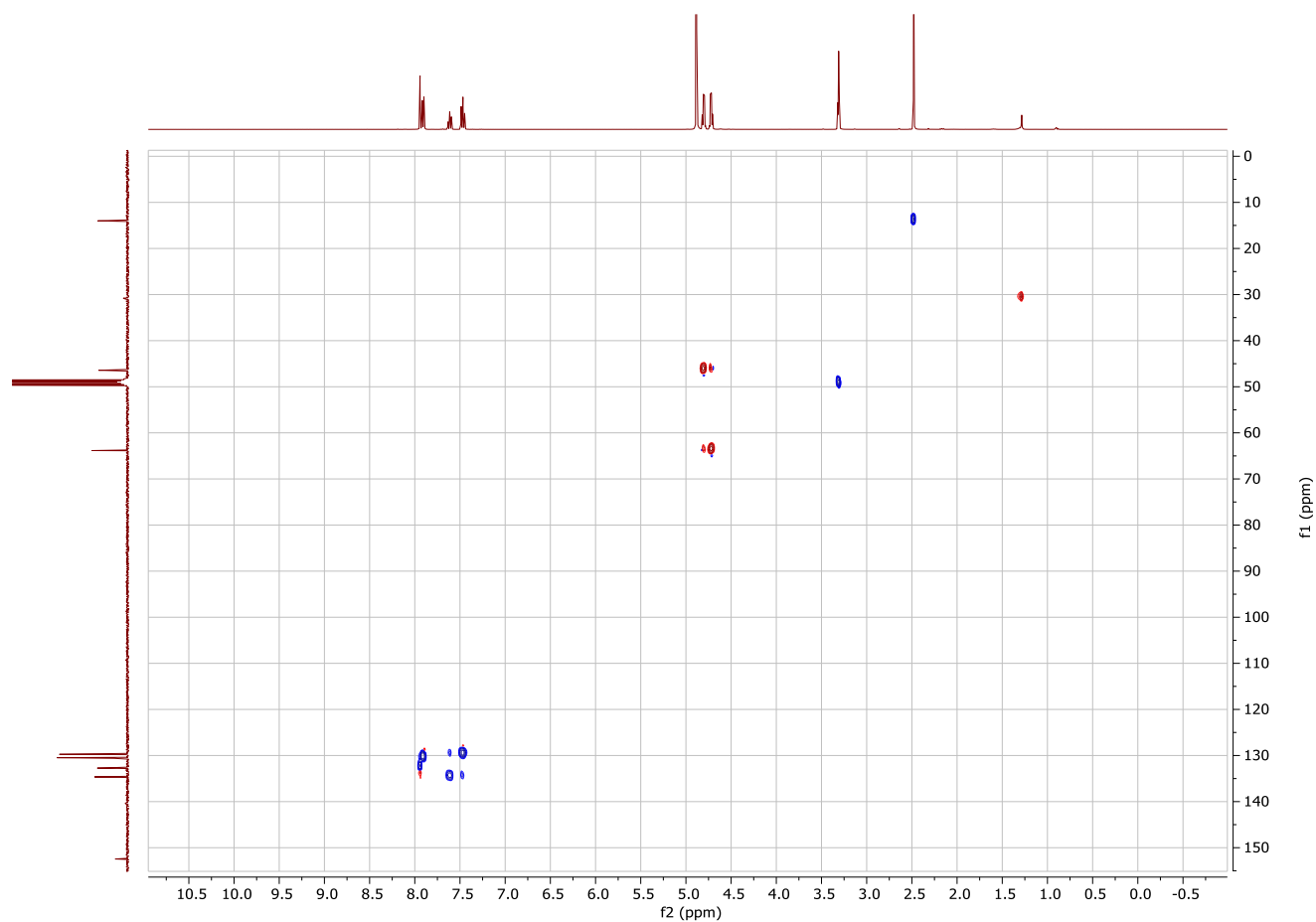


Figure S6: ^1H - ^1H -COSY NMR spectrum (400 MHz, d_4 -MeOH) of the sample QMC266

Bold lines in the depicted chemical formula visualize the observed COSY-correlations.

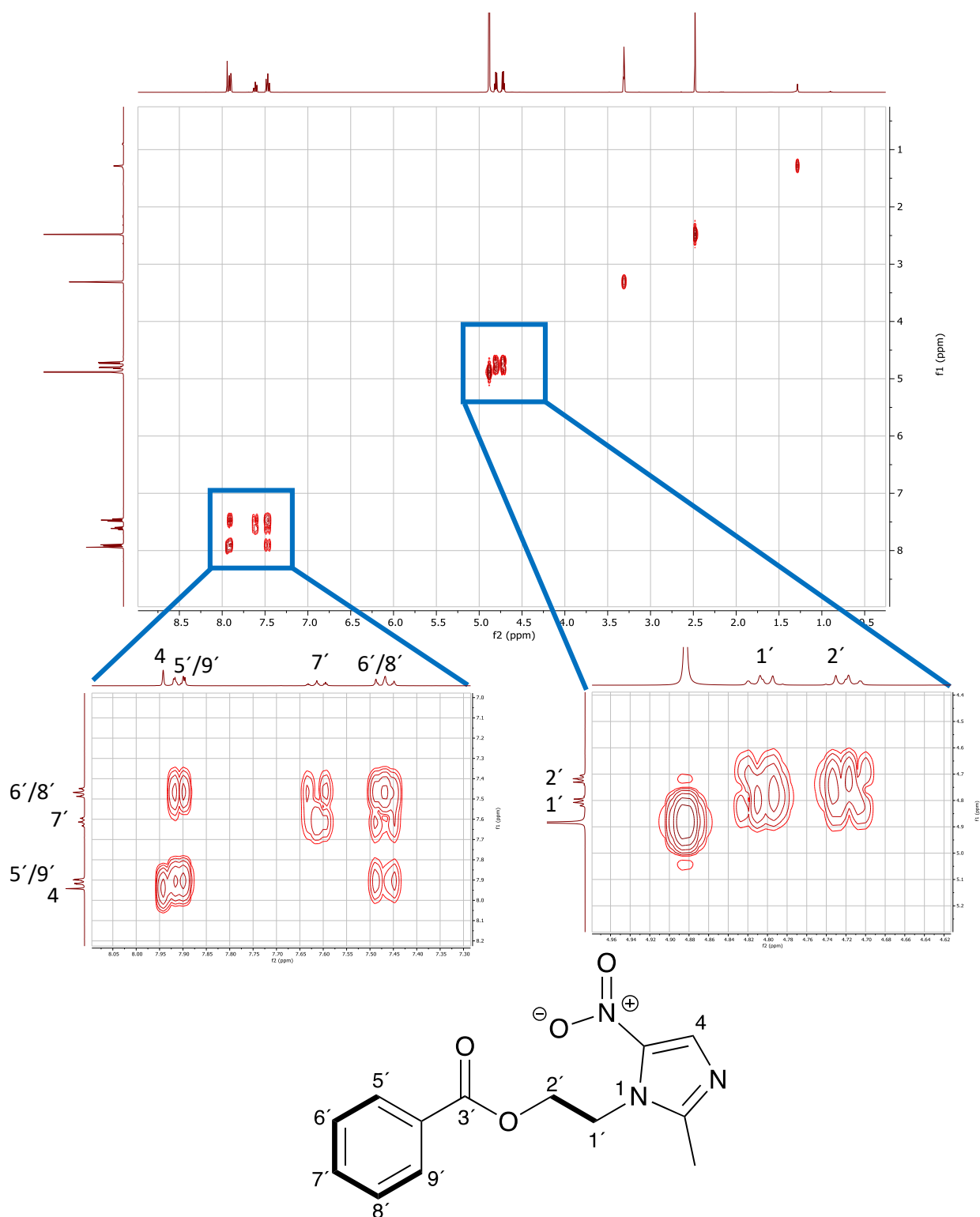


Figure S7: ^1H - ^{13}C -HMBC NMR spectrum (400 MHz, d_4 -MeOH) of the sample QMC266

Red arrows in the depicted chemical structure visualize the observed 2- and 3-bond HMBC long range correlations.

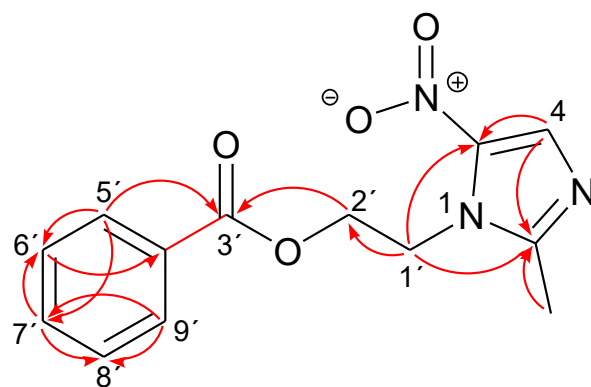
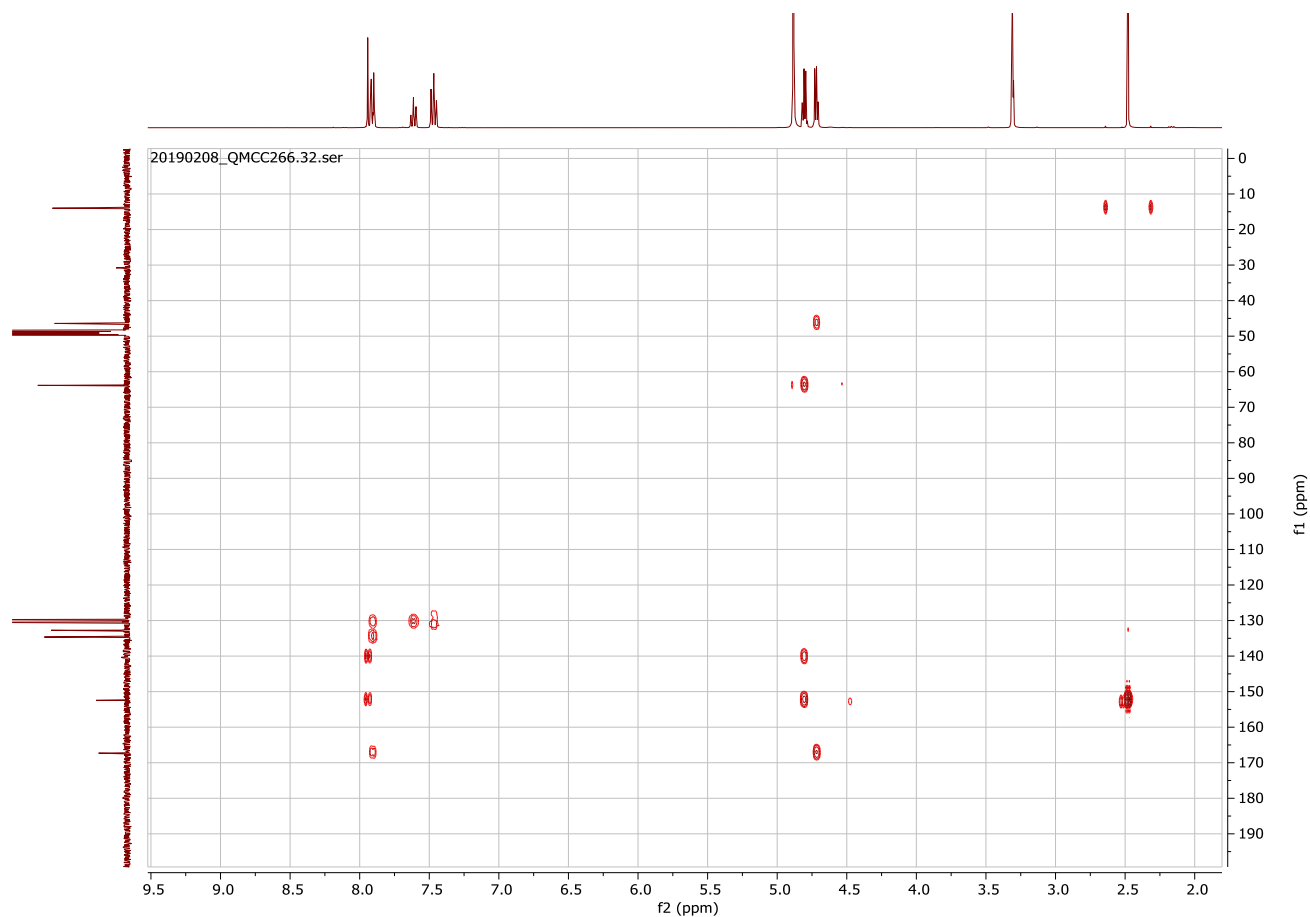


Figure S8: ^1H - ^{15}N -HMBC NMR spectrum (400 MHz, d_4 -MeOH) of the sample QMC266

Red arrows in the depicted chemical structure visualize the observed HMBC long range correlations.

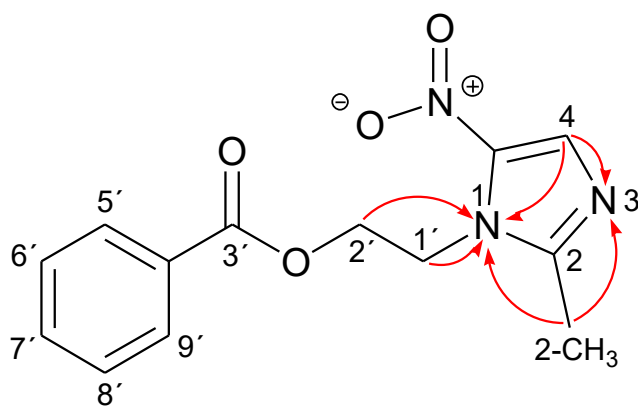
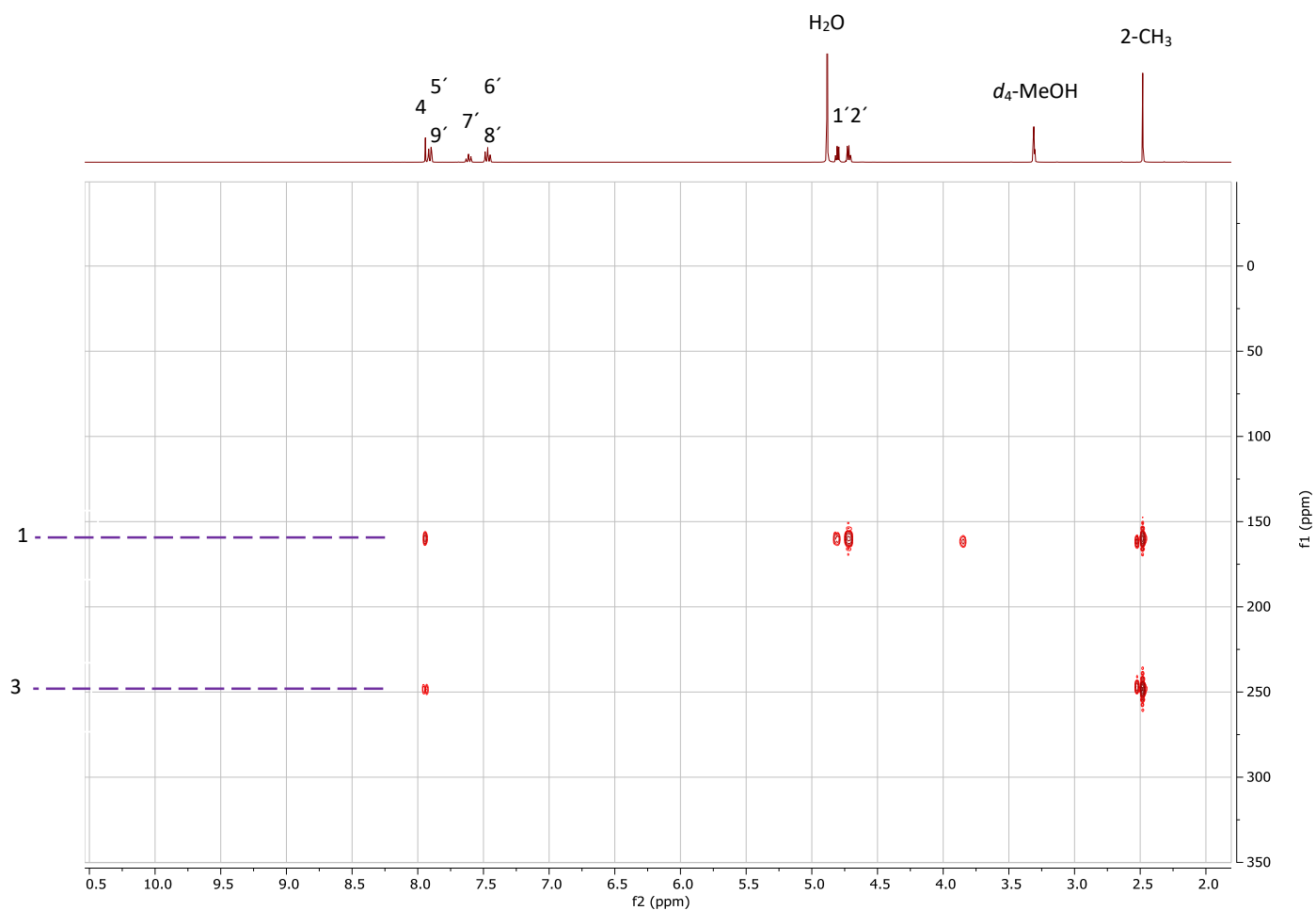


Figure S9: Superimposed ^1H NMR spectra (400 MHz, d_4 -MeOH) of a metronidazole benzoate standard and the sample QMC266 metronidazole benzoate standard depicted in red (above) and the sample QMC266 depicted in blue (below).

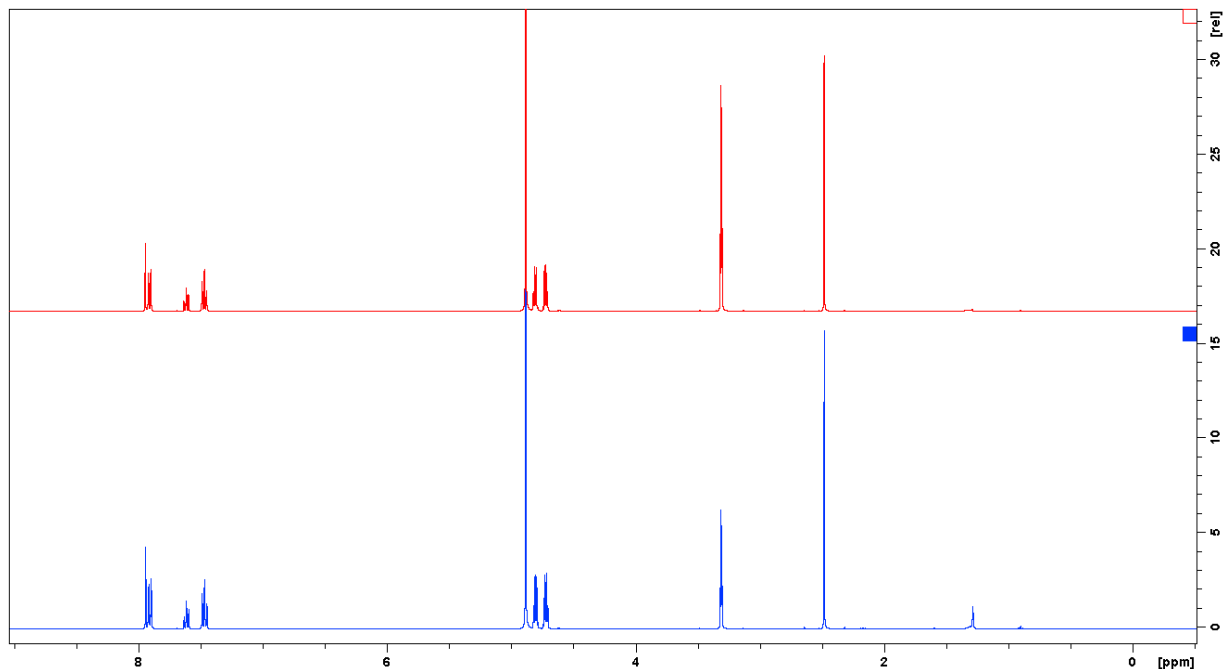


Figure S10: Superimposed ^{13}C NMR spectra (101 MHz, d_4 -MeOH) of a metronidazole benzoate standard and the sample QMC266 metronidazole benzoate standard depicted in red (above) and the sample QMC266 depicted in blue (below).

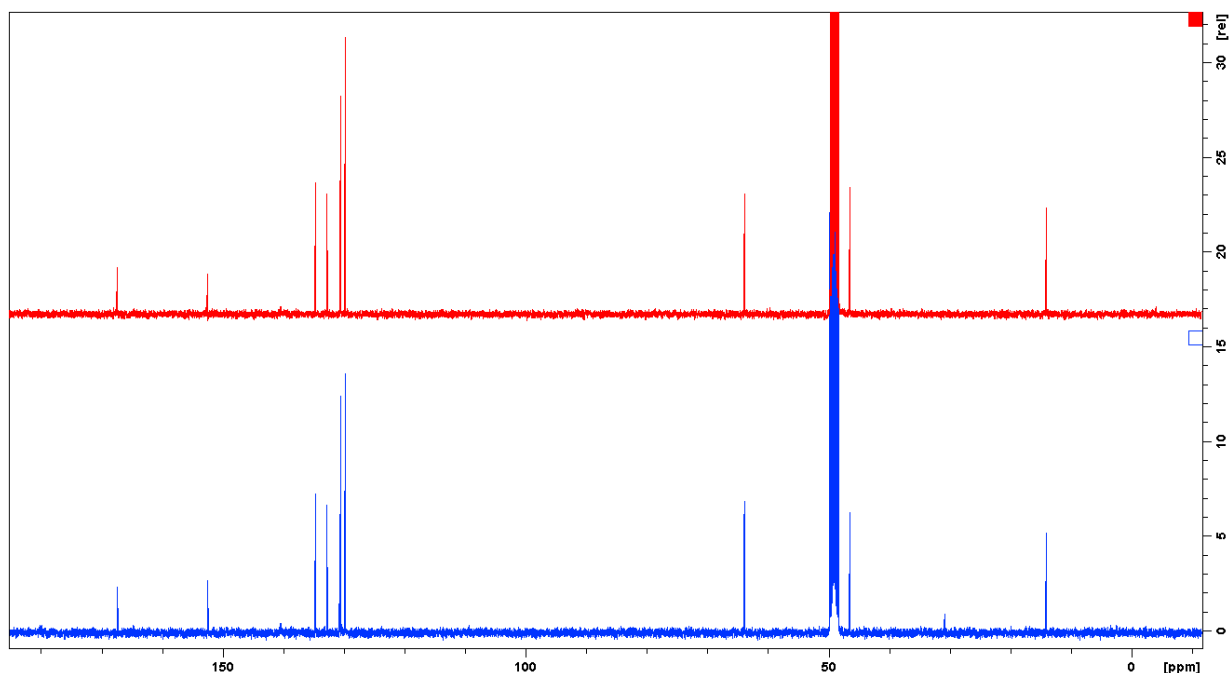
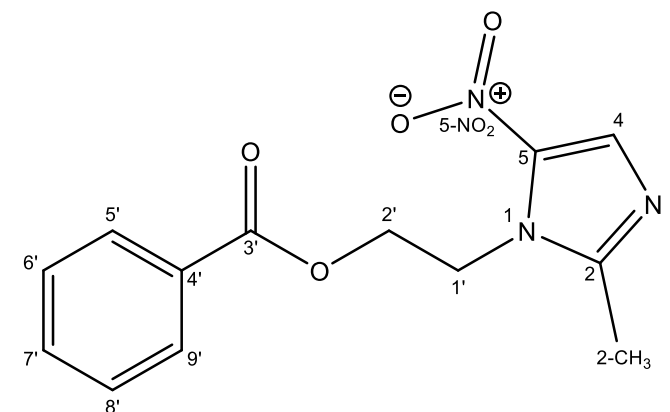


Figure S11: NMR Results for metronidazole benzoate in sample QMC266 collected in the DR Congo

Position	$\delta_{C/N}^a$	δ_H (integral, multiplicity) ^b	COSY	HMBC ^c
1	160.0 N _t			
2	152.4 C _q			
2-CH ₃	14.0 CH ₃	2.48 (3H, s)		1, 2, 3
3	248.3 N _t			
4	132.7 CH	7.94 (1H, s)		1, 2, 3, 5
5	140.5 C _q ^d			
5-NO ₂	n.o. ^e			
1'	46.4 CH ₂	4.81 (2H, m)	2'	1, 2', 2, 5
2'	63.8 CH ₂	4.72 (2H, m)	1'	1, 1', 3'
3'	167.3 CO			
4'	130.6 C _q			
5'/9'	130.5 CH	7.90+7.92 (2H, m)	6', 8'	3', 7', 5', 9'
6'/8'	129.7 CH	7.47 (2H, m)	5', 7', 9'	4', 6', 8'
7'	134.6 CH	7.61 (1H, m)	6', 8'	6', 8'



2'-(2-methyl-5-nitro-1*H*-imidazol-1-yl)ethyl benzoate

^a Recorded at 101 MHz for ¹³C. ¹⁵N NMR values were extracted from the corresponding ¹H-¹⁵N HMBC NMR spectrum.

Multiplicity determined by an edited ¹H-¹³C HSQC and a DEPT135 NMR experiment.

^b Recorded at 400 MHz.

^c Protons showing long-range correlation with indicated carbon or nitrogen.

^d ¹³C NMR value was extracted from a ¹H-¹³C HMBC NMR spectrum.

^e Not observed.

Figure S12: Content of the active pharmaceutical ingredient determined for each sample, sorted by different categories

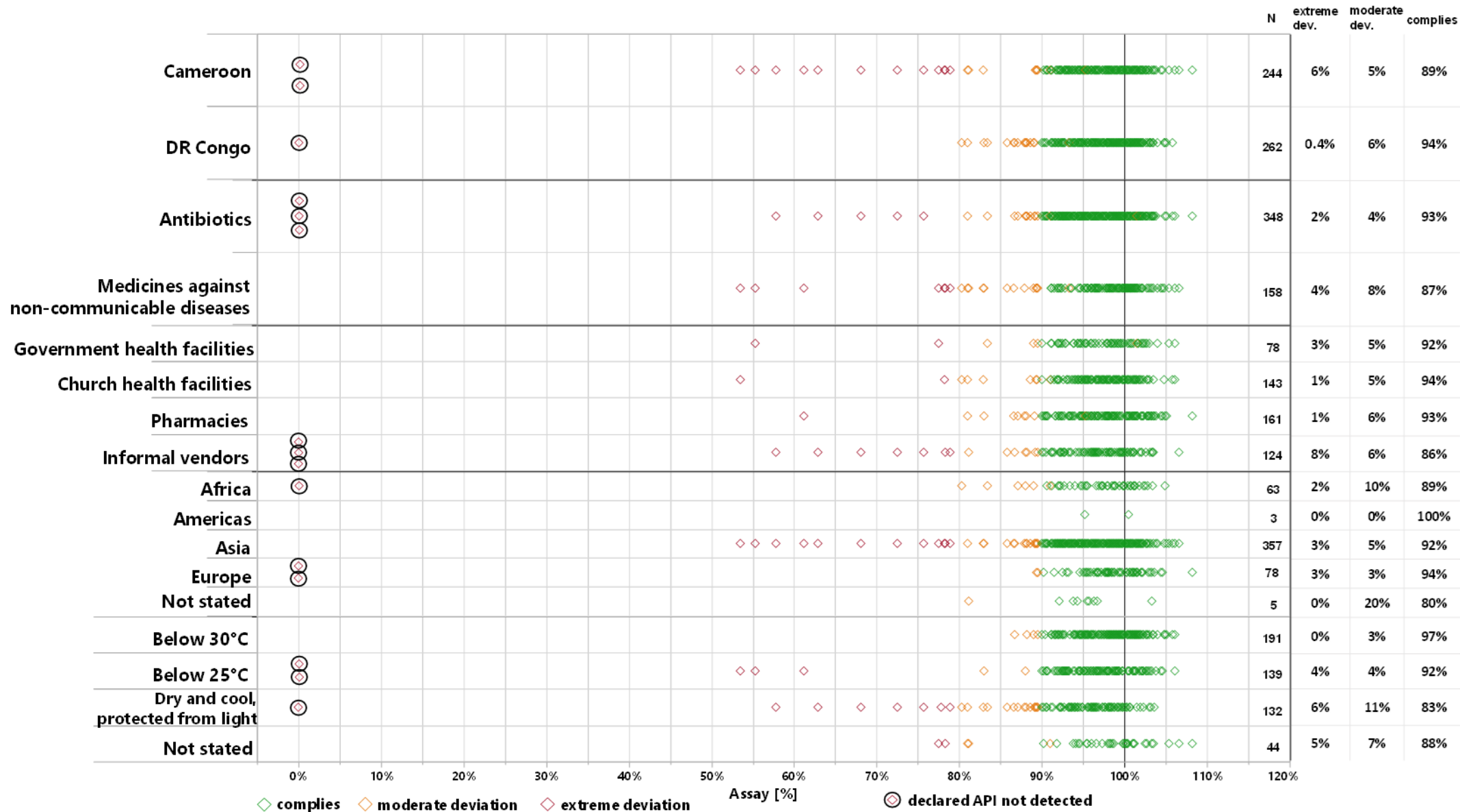


Figure S13: Dissolution of the active pharmaceutical ingredient determined for each sample, sorted by different categories

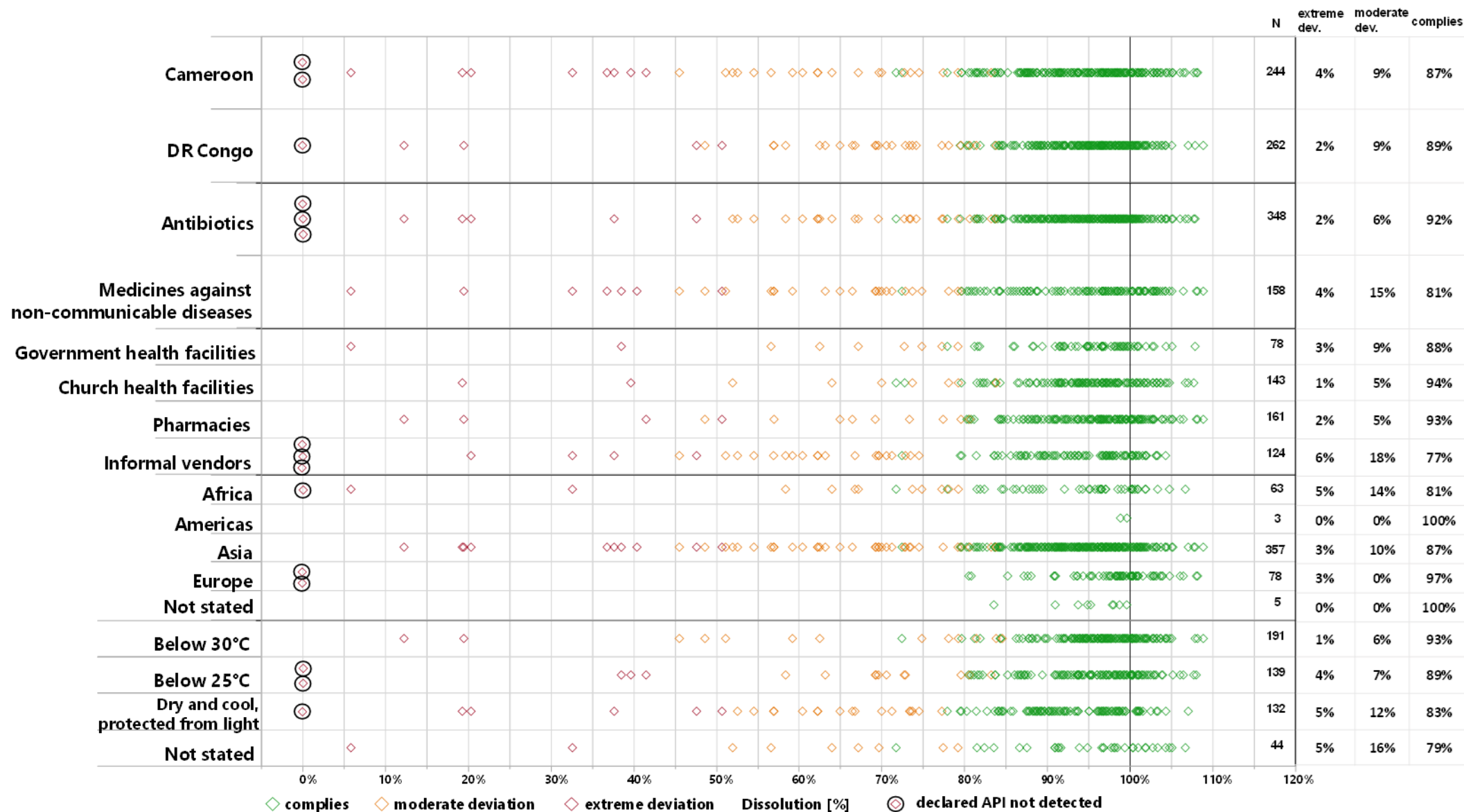


Figure S14: Frequency of non-compliance in Minilab TLC and disintegration testing in different subgroups of medicines

brand	Cameroon						DR Congo					
	N total	non-compliant total			only disintegration only TLC		non-compliant total			only disintegration only TLC		
continent of origin	N	[%]	95% CI	N	N	N	[%]	95% CI	N	N		
Generics	117	10	9%	[5-15]	2	8	4	4%	[2-10]	4	0	
Branded	108	11	10%	[6-17]	6	5	3	3%	[1-8]	2	1	
Originator	18	2	11%	[3-33]	1	1	0	0%		0	0	
Africa	23	4	17%	[8-42]	2	2	1	3%	[1-16]	0	1	
Americas	3	0	0%		0	0	6	4%	[2-8]	6	0	
Asia	155	12	8%	[4-13]	4	8	0	0%		0	0	
Europe	57	6	11%	[6-23]	3	3	0	0%		0	0	
Not stated	5	1	20%	[2-44]	0	1	3	5%	[2-15]	2	1	
Government health facilities	36	4	11%	[4-25]	0	4	42	3	7%	[3-19]	3	0
Church health facilities	71	4	6%	[2-14]	2	2	40	0	0%		0	0
Pharmacies	70	7	10%	[5-19]	4	3	70	1	1%	[0-8]	1	0
Informal vendors	66	8	12%	[6-22]	3	5	56	3	5%	[2-15]	2	1
Antibiotics	151	14	9%	[6-15]	5	9	157	6	4%	[2-8]	5	1
MANCD	92	9	10%	[5-18]	4	5	51	1	2%	[0-10]	1	0
Below 25 °C	89	10	11%	[6-20]	4	6	43	1	2%	[0-12]	0	1
Below 30°C	51	2	4%	[1-13]	1	1	102	5	5%	[2-11]	5	0
Dry and cool, protected from light	61	6	10%	[5-20]	3	3	61	1	2%	[0-9]	1	0
Not stated	42	5	12%	[5-25]	1	4	2	0	0%		0	0
Amoxicillin and Clavulanic acid	19	1	5%	[1-25]	0	1	11	0	0%		0	0
Amoxicillin	24	1	4%	[1-20]	0	1	25	0	0%		0	0
Ciprofloxacin	25	1	4%	[1-20]	0	1	26	0	0%		0	0
Doxycycline	22	0	0%		0	0	20	2	10%	[2.8-30]	2	0
Metronidazole	25	4	16%	[6-35]	4	0	27	4	15%	[6-33]	3	1
Penicillin V	13	2	15%	[4-42]	0	2	21	0	0%		0	0
Sulfamethoxazole and Trimethoprim	23	5	22%		1	4	27	0	0%		0	0
Atenolol	0	0	0%		0	0	5	1	20%	[4-62]	1	0
Furosemide	17	0	0%		0	0	18	0	0%		0	0
Glibenclamide	19	0	0%		0	0	0	0	0%		0	0
Hydrochlorothiazide	21	0	0%		0	0	4	0	0%		0	0
Metformin	20	4	20%	[8-42]	4	0	10	0	0%		0	0
Salbutamol	15	5	33%	[15-58]	0	5	14	0	0%		0	0
Overall	243	23	9%	[6.4-13.8]	9	14	208	7	3%	[1.6-6.8]	6	1

TLC= thin-layer chromatography

Table S1: List of stated manufacturers of samples investigated in this study, and results for USP 41 assay and dissolution testing

Stated Continent of Origin	Stated Country of Origin	Stated Manufacturer	N	complies	moderate deviation	extreme deviation
Africa	Benin	Pharmaquick	7	5	0	2
	Burundi	Société industrielle Pharmaceutique (SIPHAR)	1	1	0	0
	Cameroon	Africure Pharmaceuticals Cameroon S.A.	2	1	1	0
		Cinpharm **	3	2	1	0
	DR Congo	Phatkin B.P.	5	2	3	0
		Zenufa Laboratoire	4	3	1	0
	Ghana	Entrance Pharmaceuticals & Research Centre	5	3	2	0
	Kenya	Cosmos Limited	1	1	0	0
		DAWA Limited	7	6	1	0
		Elys Chemical Industries Ltd.	3	2	1	0
		Laboratory & Allied Ltd.	2	2	0	0
		MAC'S Pharmaceuticals Ltd.	2	1	0	1 ^s
		Pharmaceutical Manufacturing Co. Ltd.	1	0	1	0
		Regal Pharmaceuticals Ltd.	5	5	0	0
	Nigeria	New Divine Favour Pharmaceutical Industries Ltd.	1	1	0	0
	Senegal	Wintrop Pharma Sénégal Group SANOFI	1	1	0	0
	Togo	Sprukfield	4	4	0	0
	Uganda	Kampala Pharmaceutical Industries	7	7	0	0
Uganda	Rene Industries Ltd.	2	2	0	0	
subtotal			63	49	11	3
Americas	British West Indies	Prost Pharma (France)	2	2	0	0
	USA	Sandoz	1	1	0	0
	subtotal			3	3	0

Stated Continent of Origin	Stated Country of Origin	Stated Manufacturer	N	complies	moderate deviation	extreme deviation
Asia	China	Anhui Chengshi Pharmaceutical Co. Ltd	1	1	0	0
		Anhui Medipharm Co. Ltd.	1	0	1	0
		Chifeng Wanze Pharmaceutical Co. Ltd.	1	1	0	0
		CSPC Ouyi Pharmaceutical Co. Ltd.	22	21	1	0
		CSPC Zhongnuo Pharmaceuticals Co. Ltd.	10	10	0	0
		Farmasino Pharmaceutical Co. Ltd	6	5	1	0
		Greenfield Pharmaceuticals (Jiang Su) Co. Ltd.	1	1	0	0
		Guilin Pharmaceutical Co. Ltd.	4	4	0	0
		Jiangsu Pengyao Pharmaceutical Co. Ltd.	2	2	0	0
		Jiangsu Ruinian Qianjin Pharm. Co.Ltd	4	4	0	0
		Jiangxi Xier Kangtai Pharmaceutical Co. Ltd.	5	3	2	0
		Jinzhou Jiuyang Pharmaceutical Co. Ltd	3	2	0	1
		JSPY Pharmaceutical Co. Ltd.	3	3	0	0
		Nanjing Baijingyu Pharmaceutical Co. Ltd.	3	3	0	0
		Nanjing Sino Pharmaceutical Ltd.	1	1	0	0
		Ningbo Shuangwei Pharmaceutical Co. Ltd	6	6	0	0
		North China Pharmaceutical Co. Ltd. ***	8	8	0	0
		Reyoung Pharmaceutical Co. Ltd.	9	9	0	0
		Shandong Shenglu Pharmaceutical Co. Ltd	4	0	0	4
		Shandong Xier Kangtai Pharm Co. Ltd	1	1	0	0
		Shandong Yikang Pharmaceutical Co. Ltd.	2	1	1	0
		Shanghai Juchen Import and Exports Co. Ltd.	4	4	0	0
		Shanxi Lianbang Pharmaceutical Co. Ltd.	2	2	0	0

Stated Continent of Origin	Stated Country of Origin	Stated Manufacturer	N	complies	moderate deviation	extreme deviation
		Sinochem Jiangsu Co. Ltd	14	8	3	3
		Sishui xier Kang Pharmaceutical Co. Ltd	1	0	0	1
		Yanzhou Xierkangtai pharmaceutical Co. Ltd.	3	2	1	0
	Hong Kong	Hongkong Prost Medicines and Health Products Co. Ltd	3	3	0	0
	India	Agog Pharma Ltd.	4	4	0	0
		Alkem Laboratories Ltd.	1	0	1	0
		Arco Pharma Pvt. Ltd	7	1	6	0
		Asence Pharma Pvt. Ltd.	6	4	2	0
		Astra Lifecare Pvt. Ltd.	11	9	0	2
		Aura pharmaceuticals Pvt. Ltd	9	5	4	0
		Aurobindo Pharma Ltd.	1	0	1	0
		Axon Drugs Pvt. Ltd.	1	1	0	0
		Bliss GVS Pharma Ltd.	1	0	1	0
		Cadila Healthcare Ltd.	1	1	0	0
		Cipla Ltd.	1	1	0	0
		Ciron Drugs and Pharmaceuticals Ltd.	2	2	0	0
		Combitic Global Caplet Pvt. Ltd.	1	1	0	0
		Fourrts	3	3	0	0
		Global Pharma Healthcare Pvt. Ltd.	4	4	0	0
		Holden Medical Laboratories Pvt. Ltd.	3	3	0	0
		Intermed	1	1	0	0
		Ipca Laboratories Ltd.	1	1	0	0
		J. B. Chemicals and Pharmaceuticals Ltd.	1	1	0	0
		Kopran Limited	2	2	0	0
Leben Laboratories Pvt. Ltd		1	1	0	0	
Lincoln Pharmaceuticals Ltd.	8	8	0	0		
Lord Lifescience Pvt. Ltd.	1	0	1	0		
Macleods Pharmaceuticals Ltd.	4	4	0	0		
Mancare pharmaceutical Ltd	4	4	0	0		

Stated Continent of Origin	Stated Country of Origin	Stated Manufacturer	N	complies	moderate deviation	extreme deviation
		Maneesh Pharmaceuticals Ltd	1	1	0	0
		Maxheal Laboratories Pvt. Ltd.	2	1	1	0
		Maxtar Bio-Genics	14	9	2	3 *
		Medicamen Biotech Ltd.	8	7	1	0
		Medicef Pharma	4	4	0	0
		Medico Remedies Pvt. Ltd.	5	0	1	4
		Medley Pharmaceuticals Ltd.	5	5	0	0
		Medopharm Pvt. Ltd.	41	39	2	0
		Mepro Pharmaceuticals Pvt. Ltd.	2	2	0	0
		Micro Labs Ltd.	4	4	0	0
		Milan Laboratories (India) Pvt. Ltd	6	5	1	0
		Nem Laboratories Pvt. Ltd.	1	1	0	0
		not stated	1	1	0	0
		Osaka Pharmaceuticals Pvt. Ltd.	3	1	2	0
		PIL Pharmaceuticals Pvt. Ltd.	1	1	0	0
		Prashi Pharma Pvt. Ltd	6	1	4	1
		Shalina Laboratories Pvt. Ltd.	1	1	0	0
		Sparsh Bio-Tech Pvt. Ltd.	7	7	0	0
		Strides Arcolab Limited	23	21	2	0
		Strides Shasun Limited	11	9	2	0
		Triveni Formulations Limited	1	1	0	0
		Ultra Care International	2	2	0	0
	UMEDICA Laboratories	1	1	0	0	
	Zee Laboratories	1	1	0	0	
	ZIM Laboratories Ltd.	1	1	0	0	
Sultanat of Oman	National pharmaceutical industries	1	1	0	0	
Turkey	Bilim Pharmaceuticals	1	1	0	0	
subtotal			357	294	44	19
Europe	Austria	Sandoz	10	10	0	0
	Belgium	Merck	3	3	0	0
		Oxford Pharma	1	0	0	1 ⁵
	Cyprus	Medochemie Ltd.	2	2	0	0

Stated Continent of Origin	Stated Country of Origin	Stated Manufacturer	N	complies	moderate deviation	extreme deviation
		Remedica Ltd	2	2	0	0
	France	Famar Lyon	1	1	0	0
		Glaxo Welcome Production	3	3	0	0
		Laboratoires Bailleul	1	1	0	0
		Laboratoire Bailly-Creat	6	6	0	0
		Sanofi-Winthrop Industrie	6	6	0	0
		Germany	Aspen Bad Oldesloe GmbH	1	1	0
	Berlin Chemie		1	1	0	0
	Denk Pharma GmbH & Co. KG		12	10	2	0
	Salutas Pharma GmbH		2	2	0	0
	Italy	Errekappa Euroterapici S.p.A	1	1	0	0
		Laboratori Guidotti S.p.A	1	1	0	0
	Spain	Ferrer Internacional S.A.	3	3	0	0
		Novartis Farmacéutica S.A.	14	14	0	0
	Sweden	Bluefish Pharmaceuticals AD	1	1	0	0
	United Kingdom	SmithKline Beecham Pharmaceuticals	1	0	0	1 [§]
		Sonmart Pharma (UK)	6	6	0	0
	subtotal		78	74	2	2
not stated	not stated	Cinpharm **	3	3	0	0
		not stated	2	1	1	0
	subtotal		6	5	1	0
total			506	424	58	24

* Two of these three samples had been expired at the date of collection.

** Cinpharm recently became a Cameroonian company. However, three samples did not state the country of manufacture, therefore these three samples were listed in the category "not stated".

*** The name of this manufacturer was given on different samples as "North China Pharmaceutical Co. Ltd.", or as "NCPC, PRC", or as "NCPC North Best". Since all of them appear to have the same contact address, they were considered in this study as a single manufacturer.

[§] Falsified medicine; poor quality can not be attributed to the stated manufacturer.

Table S2: List of samples reported to fail GPHF Minilab TLC analysis, and of samples reported to pass GPHF Minilab TLC analysis but showing extreme deviations in USP assay testing, with their respective USP assay results

Sample ID	API	USP assay classification	USP assay result [%]
1) Samples reported to <u>fail</u> GPHF Minilab TLC analysis:			
QMCA241	Amoxicillin / clavulanic acid	extreme deviation	0% / 0%
QMC266	Metronidazole	extreme deviation	0%
QMCA035	Penicillin V	extreme deviation	0%
QMCA001	Salbutamol	extreme deviation	54%
QMCA025	Salbutamol	extreme deviation	55%
QMCA215	Salbutamol	extreme deviation	61%
QMCA072	Salbutamol	deviation	81%
QMCA074	Sulfamethoxazole / Trimethoprim	deviation	91% / 95%
QMCA019	Sulfamethoxazole / Trimethoprim	complies	99% / 98%
QMCA212	Sulfamethoxazole / Trimethoprim	complies	102% / 100%
QMCA082	Sulfamethoxazole / Trimethoprim	complies	103% / 100%
QMCA032	Amoxicillin	complies	92%
QMCA210	Penicillin V	complies	93%
QMCA084	Salbutamol	complies	94%
QMCA184	Ciprofloxacin	complies	95%
2) Samples reported to <u>pass</u> GPHF Minilab TLC analysis but showing extreme deviations in USP assay testing:			
QMCA253	Penicillin V	extreme deviation	58%
QMCA107	Penicillin V	extreme deviation	68%
QMCA244	Penicillin V	extreme deviation	73%
QMCA177	Penicillin V	extreme deviation	76%
QMCA168	Salbutamol	extreme deviation	78%
QMCA179	Salbutamol	extreme deviation	78%
QMCA191	Salbutamol	extreme deviation	78%
QMCA239	Salbutamol	extreme deviation	79%

Table S3: Compendial quality results for the different products and batches as stated on the packaging

See separate pdf file