

Final Campaign report

Development of scalable process for the synthesis of MK-4482/EIDD-2801/ Molnupiravir via chemical route

Submitted to

B. Frank Gupton, PhD

Floyd D. Gottwald Chair of Pharmaceutical Engineering

Department Chair, Chemical and Life Science Engineering

Virginia Commonwealth University

Medicines for All Institute

Contact: M4ALL@vcu.edu



TCG Life sciences Pvt. Limited –A Contract development and manufacturing organization (CDMO)

Report prepared by Dr. Sarabindu Roy & Dr Ajay K. Yadaw

Scientists associated with the project from TCG LS:

S.N.	Name of Scientist	Designation
1	Dr. Subho Roy	Vice Presedent-Chemistry
2	Dr. Ajay K. Yadaw	Director – Chemistry
3	Dr. Sarabindu Roy	Group Leader
4	Dr. Sadhanendu Samanta	Research Scientist
5	Mr. Seelam Balaji Reddy	Research Scientist
6	Mr. Appana Ramakrishna	Senior Research Chemist

Scientists associated from TCG Green site:

S.N.	Name of Scientist	Designation
1	Dr. Chris Senanayake	CEO
2	Dr. Joseph Armstrong	COO
3	Dr. Gopal Sirasani	Director, Operations and Business Development

Table of contents:

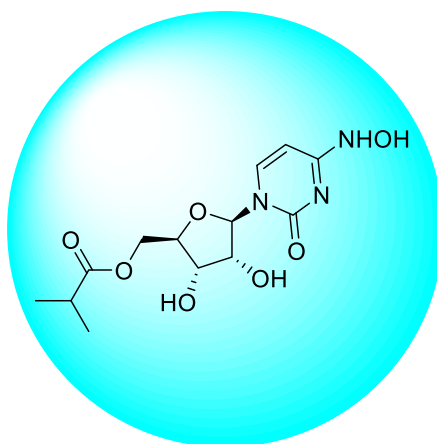
S.N.	Details
1.	Major Scope / Overview of the project
2	Summary of work done and major accomplishments
3	Final developed scheme and Protocol
4	Results & Discussion
5	Safety study and conclusion
6	Further areas of development / improvements
7	Acknowledgement

Major Scope of the work:

- ❖ Feasibility study of the proposed route
- ❖ Analytical method development for in-process control and release of the intermediates as well as final compound
- ❖ Optimization of the reaction in terms of yield, quality & reaction time
- ❖ Comprehensive safety studies of the optimized protocol by DSC
- ❖ Identification of key process impurities / Impurity profiling
- ❖ Scale up of the target compound to kg scale
- ❖ Preparation of Lab development report

Overview:

MK-4482/EIDD-2801/Molnupiravir is a final API and an antiviral with emerging potential to treat COVID-19. Structure of the Target compound is shown below. Herein chemical non-enzymatic scalable synthesis of the MK-4482/EIDD-2801/Molnupiravir is described.



Summary of work done and major accomplishments

- ❖ Various conditions were screened for all the steps and based on the study a safe and scalable protocol has been established for the synthesis of target compound in Kg scale
- ❖ Several process impurities have been identified, isolated, synthesized and characterized
- ❖ Efficient purification protocol has been established to purge most of the process impurities
- ❖ Preliminary safety assessment of the SM, isolated intermediates and final target compound have been performed using DSC Using optimized process eventually final target compound has been synthesized on kg scale with chemical purity >99.5% (A%) and with Assay 99.4%



Certificate of Analysis of scale up batch

CERTIFICATE OF ANALYSIS

Product Name : ((2R,3S,4R,5R)-3,4-dihydroxy-5-(4-(hydroxyamino)-2-oxopyrimidin-1(2H)-yl)tetrahydrofuran-2-yl)methyl isobutyrate/MOLNUPIRAVIR.

Batch No. : CR592-16492-32-P

Date of Mfg : AUG 2021

Quantity : 760 gm

S.No.	Test	Results	Specification
1.0	Appearance	Off white color solid	White to light yellow solid
2.0	Identification by		
	i) IR	Graph attached	IR spectrum of sample should match with the IR spectrum of standard.
3.0	Water content by KF (%w/w)	0.16 % w/w	Report the results
4.0	Residue on ignition	0.004 % w/w	Report the results
5.0	pH (1.0 % solution in water)	5.82	Report the results
6.0	Chromatographic purity by HPLC (% area)		
	i) Purity	99.80 %	Report the results
	ii) Single maximum unknown impurity	0.10 %	Report the results
7.0	Melting point by DSC	161.9°C	Report the results
8.0	Assay by HPLC (on as is basis)	99.4 % w/w	Report the results

Soumya Chatterjee
Prepared By:

Date 11 Aug 2021

Sukanta Kumar Saha
Checked By:

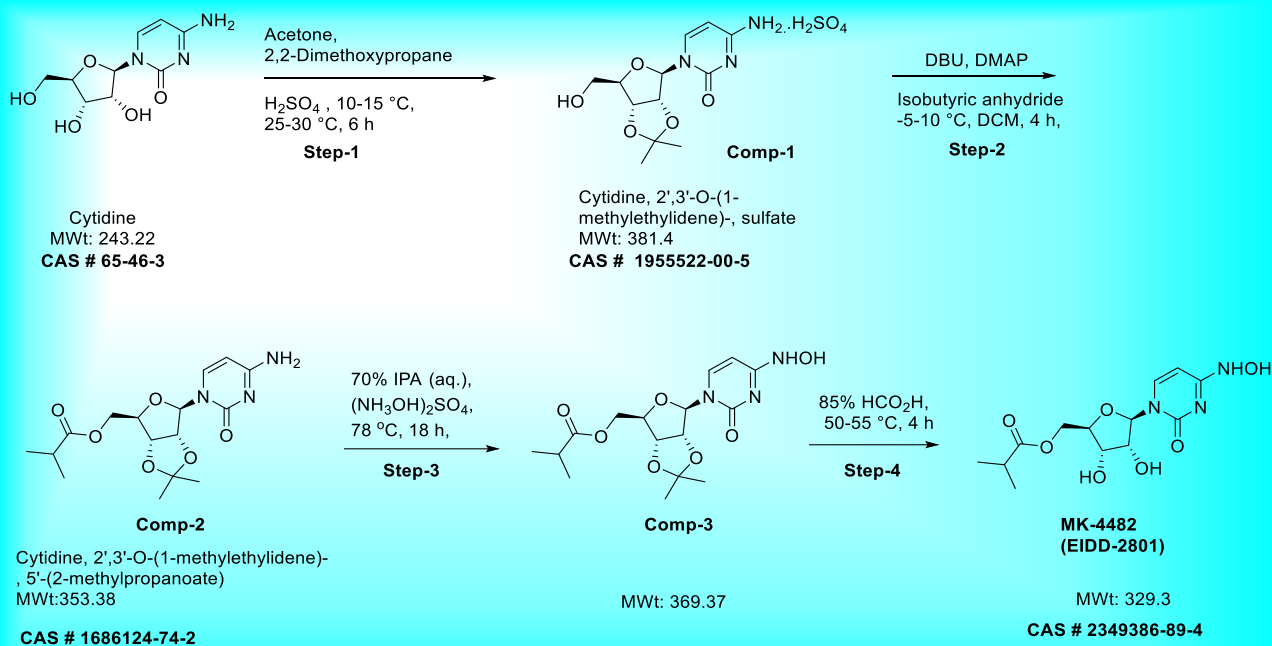
Date 11 Aug 2021

Sankhpadhyay
Approved By:

Date 11 Aug 2021.

Final optimized synthetic scheme

The final optimized synthetic scheme is shown below.



Experimental:

Step-1:

List of Raw materials

- i. Cytidine
- ii. 2,2-Dimethoxypropane
- iii. Sulfuric acid
- iv. Acetone
- v. MTBE

Process Information:-

Actual batch size and quantity (Batch No. CR592-16022-86):

S. No.	Reagent	Unit	Qty	Mol Wt.	Mole	Mole ratio/ wt. times vol	Source/Batch No.	
1	Cytidine	kg	1.0	243.22	4.11	1.0	ASUN Laboratory LTD /07-009-2021-03020	
2	2,2-Dimethoxypropane	kg	0.513	104.15	4.93	1.2	Bharat Jyothi IMPAX/ 411D2O1015022H	
3	Sulfuric acid	kg	0.483	98	4.93	1.2	Simson/K016J20	
4	Acetone	Lot-1	L	10.0	58.08	--	10.0 V	Deepak Phenolics Ltd. /10-T-3103-A
		Lot-2	L	10.0	58.08	--	10.0 V	
5	MTBE	L	5.0	--	--	5.0 V	DOR Chem. Ltd. /DOR0033190	

a) Process details:

S. No.	Procedure	Qty.	Remarks
1.	Check the cleanliness of the reaction vessel (20 L 3-necked flask) fitted with an internal temperature probe, overhead stirrer, and addition flask and nitrogen line.		
2.	Charge Acetone Lot-1 into the reaction flask under N ₂ atmosphere.	10 L	
3.	Charge Cytidine (1.0 kg) into the reaction vessel under N ₂ atmosphere.	1.0 kg	

S. No.	Procedure	Qty.	Remarks
4.	Add 2, 2-Dimethoxypropane into the reaction vessel.	0.51 kg	Time : 30 min
5.	Cooled the vessel to 10-15 °C.		
6.	Add Sulfuric acid maintaining the internal temperature of the vessel at 10-15 °C.	0.483 kg	Time : 60 min
7.	Raise the temperature up to 25-30 °C and maintain for 14 h.		
8.	Send the sample of the reaction mixture for HPLC analysis to check the consumption of Cytidine (IPC-1). Sample preparation: Take sample directly from the reaction mass and submit as such.		IPC-1 (Cytidine content area %) Result: 0.4%
9.	Filter the reaction mass under nitrogen atmosphere		
10.	Wash the solid with Acetone Lot-2 .	10 L	
11.	Again slurry-wash the solid with MTBE .	5.0 L	
12.	Dry the compound under vacuum at 50-55 °C for ~8 h till constant weight.		
13.	Send the sample for checking purity by HPLC.		Purity by HPLC area% Result: 99.70%
14.	Yield	1.58 kg	Molar yield % = Quantitative QNMR assay = 97.27 w/w%

b) In process control data:

S. No.	Batch Id	IPC-1 (Content of Cytidine area %)	Purity by HPLC area%
1	CR592-16022-86	0.4%	Attachment-1 IPC:- 97.16%

c) Result of the batch:

S. No	Batch No.	Input (kg)	Output (kg)	Assay by NMR	Assay based Yield	Analytical data
1	CR592-16022-86	1.0	1.58	97.27%	98%	Attachment-2 HPLC Area Purity: 99.70%

Similarly following batch was synthesized:

S. No	Batch No.	Input (kg)	Output (kg)	Assay by NMR	Assay based Yield	Analytical data
2	CR592-16492-3	1.0	1.54	Not performed	Quantitative	Attachment-3 HPLC Area Purity: 99.41%

Step-2:

List of Raw materials

- i) Compound-1
- ii) 1, 8-Diazabicyclo [5.4.0] undec-7-ene (DBU)
- iii) Isobutyric anhydride
- iv) DMAP
- v) DCM
- vi) Acetic acid
- vii) Process water
- viii) Sodium chloride
- ix) Sodium bicarbonate
- x) Hexane

Process Information:

Actual batch size and quantity (Batch No. CR592-16492-08):

S. No.	Reagent	Unit	Qty	Mol Wt.	Mole	Mole ratio/ wt. times vol	Source
1	Compound-1	kg	1.0	381.4	2.62	1.0 eq	CR592-16022-86
2	1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU)	kg	0.838	152.2	5.50	2.1 eq	Real chemises products (P) PTD/1361/XX/12/028
3	Isobutyric anhydride	kg	0.498	158.19	3.14	1.2 eq	Nova Phene specialties PVT. LTD/SHBJ0529
4	DMAP	kg	0.064	122.17	0.52	0.2 eq	AVRA/N2001483
5	DCM	Lot-1	10.0	-	-	10.0 V	STANDARD REAGENTS PVT LTD/SR-0150421018
		Lot-2	5.0			5.0 V	

S. No.	Reagent	Unit	Qty	Mol Wt.	Mole	Mole ratio/ wt. times vol	Source
6	Acetic acid (10%)	L	10.0	-	-	10.0 V	Rankem/ A010D21
7	Sodium bicarbonate (8% solution)	L	12.0	-	-	12.0 V	Rankem/ J148C21
8	Hexane	L	5.0			5.0 V	STANDARD REAGENTS PVT LTD/SR- 2510321057
9	Sodium chloride (saturated solution)	L	10.0			10 V	Rankem/ A010D21
10	Sodium sulfate	kg	0.5			0.5 w/w	Rankem/ J148C21

a) Process details:

S. No.	Procedure	Qty.	Remarks
1.	Check the cleanliness of the reactor-1 (20 L-4 necked RBF, fitted with an internal temperature probe, addition flask and nitrogen line).		
2.	Charge DCM Lot-1 into the reactor at 25-30 °C.	10.0 L	
3.	Charge Compound-1 into the reactor.	1.0 kg	
4.	Charge 1, 8-Diazabicyclo [5.4.0] undec-7-ene (DBU) into the reactor.	0.838 kg	
5.	Charge DMAP into the reactor.	0.064 kg	
6.	Cool the reactor to (-8±2) °C (internal temperature).		
7.	Slowly add Isobutyric anhydride at (-8±2) °C for 60-90 min.	0.498 kg	
8.	Stir the reaction mixture at 0-5 °C for 4 h.		
9.	Submit the sample to QC for HPLC. (Sample preparation: Take the reaction mass, evaporate to dryness under reduced pressure and send the sample to QC).		IPC-1: content of Comp-1 Result: 0.25%
10.	Quench the reaction with 10% Acetic acid and stir the mixture for 15 min and then separate the layers at 0-10 °C.	10.0 L	
11.	Back extract the aqueous layer with DCM Lot-2 .	5.0 L	

12.	Combine the organic layer and wash it with saturated sodium bicarbonate solution.	12.0 L	
13.	Wash the organic layer with saturated sodium chloride solution.	10.0 L	
14.	Dry the Organic layer over sodium sulfate.	0.5 kg	
15.	Distill out the organic layer under vacuum at 35-40 °C.		
16.	Charge Hexane over the solid and stir the mixture until free solid appeared and filter the compound under nitrogen atmosphere.	5.0 L	
17.	Dry the compound under vacuum at 40-45 °C for 5 h.		
18.	Send the sample for checking purity by HPLC.		Purity by HPLC Area% Result: 93.83%
19.	Yield (w/w)	0.882 kg	Molar yield % = 95 HPLC assay = 88.9 w/w%

b) In process controls data:

S. No.	Batch Id	IPC-1 (Content of compound-1 by HPLC A%)	Purity by HPLC
1	CR592-16492-8	Result: 0.25%	Attachment-4

c) Results of the batch:

S. No	Batch No.	Input (kg)	Output (kg)	Molar Yield on as is basis	Analytical data
1	CR592-16492-8	1.0	0.882	95.21%	Attachment-5 Comp-2: 93.83%; Di-acyl impurity @ 1.43 RRT: 5.15%
2	CR592-16492-4	0.5	0.437	94.38%	Attachment-6 Comp-2: 94.59%; Di-acyl impurity @ 1.43 RRT: 4.69%
3	CR592-16492-7	0.5	0.439	94.76%	Attachment-7 Comp-2: 94.37%; Di-acyl impurity @ 1.43 RRT: 4.97%

Step-3:

List of Raw materials

- i. Compound-2
- ii. Hydroxylamine sulfate
- iii. Isopropyl alcohol
- iv. Isopropyl acetate
- v. Water
- vi. DMAP
- vii. Saturated NaCl solution
- viii. Sodium sulfate (anhydrous)

Process Information:

Actual batch size and quantity:

S. No.	Reagent	Unit	Qty	Mol Wt.	Moles	Mole ratio/ wt. times vol	Source
1	Compound-2	kg	1.0	353.2	2.83	1.0	CR592-16492-8 (850.0 g) + CR592-16492-7 (150.0 g)
2	Hydroxylamine sulfate	kg	0.697	164.14	4.24	1.5	BASF/214671752 0
3	DMAP	kg	0.041	122.14	0.33	0.12	AVRA/ N2001483
3	Isopropyl alcohol (70%)	L	10.0			10.0 V	UNID Global Corp/2001IPA- 003
4	Isopropyl acetate	Lot-1	10			10.0 V	
		Lot-2	2.5			2.5 V	
		Lot-3	0.5			0.5 V	
5	Water	L	5.0			5.0 V	In-house
6	Saturated NaCl solution	L	5.0			5.0 V	Rankem/J191K20
7	Sodium sulfate (anhydrous)	kg	0.5			0.5 w/w	Rankem/J015B21

a) Process details:

S. No.	Procedure	Qty.	Remarks
1.	Check the cleanliness of the Reactor-1 (20 L-4 necked RBF, fitted with an internal temperature probe).		
2.	Charge Isopropyl alcohol-water (70:30) into the reactor at 25-30 °C.	10 L	
3.	Charge Compound-2 into the reactor at 25-30 °C.	1.0 kg	
4.	Charge DMAP into the reactor at 25-30 °C.	0.041 kg	
5.	Charge Hydroxylamine sulfate into the reactor at 25-30 °C.	0.697 kg	
6.	Heat the reactor to (80±5) °C (internal temperature).		
7.	Stir the reaction mixture at 80-85 °C for 18 h.		
8.	Submit the sample to QC for HPLC. (Sample preparation: Stop the stirring, settle the reaction mass and take the upper IPA layer and submit as it is.)		IPC: Content of Compound-2 by HPLC A% Result: 2.69%
9.	Cool the reactor at 25-30 °C.		
10.	Separate the layers and distil out the IPA layer completely under vacuum at 50-55 °C.		
11.	Charge water into the residue.	5.0 L	
12.	Charge Isopropyl acetate Lot-1 into the mixture.	10.0 L	
13.	Stir the mixture for 15 min.		
14.	Separate the layers, wash the organic layer with saturated NaCl solution.	5.0 L	
15.	Take the organic layer and dry it over anhydrous sodium sulfate.	0.5 kg	
16.	Distill the organic layer under vacuum at 50-55 °C to get solid crude compound.		
Purification :			
17.	Take the above solid crude compound into the reactor.		
18.	Charged Isopropyl acetate Lot-2 into the reactor.	2.5 L	
19.	Heat the reactor to (80±5) °C (internal temperature).		
20.	Stir the reaction mixture at 80-85 °C for 2 h.		Clear solution
21.	Cool the reactor to 0-5 °C (internal temperature).		

22.	Stir the reaction mixture at 0-5 °C for 8 h.		
23.	Filter the compound and wash it with chilled (0-5 °C) Isopropyl acetate Lot-3.	0.5 L	
24.	Dry the compound at 45-50 °C in vacuum tray dryer (VTD) under reduced pressure NLT 640 mm of Hg for 6 h till constant weight.		
25.	Send the sample for analysis.		Purity by HPLC NLT 97% Result: 98.69%
26.	Yield.	740 g	Molar yield % = 70.7 HPLC assay = 96.6 w/w%

b) In process controls data:

S. No.	Batch Id	IPC-1 Content of Compound-2 by HPLC A%	Purity by HPLC
1	CR592-16492-26	Result: 2.69%	Attachment-8

c) Results of the batch:

S. No	Batch No.	Input (kg)	Output (kg)	Molar Yield (%)	Analytical data
1	CR592-16492-26	1.0 Source: (CR592-16492-8 (850.0 g) + CR592-16492-7 (150.0 g))	0.740	70.7	Attachment-9 HPLC A%: 98.70 EIDD: 1.06%
2	CR592-16492-25	0.50 Source: (CR592-16492-4 (400.0 g) + CR592-16492-7 (100.0 g))	0.367	70.3	Attachment-10 HPLC A%: 99.13 EIDD: 0.74%
3	CR592-16492-28	0.50 Source: CR592-16492-21	0.368	70.4	Attachment-11 HPLC A%: 99.21 EIDD: 0.32%

Step-4:

List of Raw materials

- i. Compound-3
- ii. Formic acid (85%)

- iii. Ethanol
- iv. Water
- v. Acetone

Process Information

Actual batch size and quantity:

S. No.	Reagent	Unit	Qty	Mol Wt.	Mole	Mole ratio/ wt. times vol	Source
1	Compound-3	kg	1.4	369.4	3.79	1.0	CR592-16492-25 (350.0 g) + CR592-16492-26 (700.0 g) + CR592-16492-28 (350.0 g)
2	Formic acid (85%)	L	7.0	46.03		5.0 V	Real chemises products (P) LTD/389/XXI/01/029
3	Ethanol	Lot-1	L	3.5		2.5 V	Changshu Hongsheng Fine Chem. Ltd/20210405
		Lot-2		7.0		5.0 V	
4	Acetone	L	0.7			0.5 V	Deepak Phenolics Ltd/10-T3103-A
5	Water	Lot-1	L	2.8		2.0 V	In-house
		Lot-2		0.7		0.5 V	
		Lot-3		1.4		1.0 V	
		Lot-4		0.7		0.5 V	

a) Process details:

S. No.	Procedure	Qty.	Remarks
1.	Check the cleanliness of the Reactor-1 (20 L 4-necked RBF, fitted with an internal temperature probe).		
2.	Charge Compound-3 into the Reactor-1.	1.4 kg	
3.	Charge Formic acid (85%) into Reactor-1.	7.0 L	

4.	Stir the reaction mixture at 50-55 °C for 6 h.		
5.	Submit the sample to QC for HPLC. (Sample preparation: Take the reaction mass and submit as it is).		IPC-1: Content of Compound-3 by HPLC A% Result: 0.92%
6.	Distil the reaction mass under vacuum at 40-45 °C.		
7.	Co-distil the residual part with Ethanol Lot-1 at 40-45 °C.	3.5 L	
8.	Charge Ethanol Lot-2 into the reactor at 25-30 °C.	7.0 L	
9.	Heat the reactor to (80±5) °C (internal temperature).		
10.	Stir the reaction mixture at (80±5) °C for 5 h.		
11.	Distill out the ethanol u/v at 45-50 °C.	Crude:- 1.6 kg	Analysis by HPLC Result: Comp-3: 1.11%, MK-4482: 87.43%, Foramyl IMP: 0.03%, NHC: 7.81%, Imp at RT 6.80 : 0.02%
12.	Add Water Lot-1 into the residual crude to obtain a clear solution at 25-30 °C.	2.8 L	
13.	Filter the solution through 5 micron filter cloth to remove any extraneous particles.		
14.	Take the filtrate into the Reactor and stir it for 12 h at 5-10 °C.		Solid precipitate is observed
15.	Filter the solid and wash it with Water Lot-2 .	0.7 L	
16.	Dry the solid compound under vacuum suction for 3 h.		Analysis by HPLC Result: SM: 0.46%, MK-4482: 98.62%, NHC: 0.83%, Weight: 940.0 g, KF = 11.0 w/w%
<u>Purification</u>			
17.	Take the above crude solid compound into the 3L RBF.		
18.	Charge water Lot-3 into the RBF.	1.4 L	
19.	Heat the mixture at 75-80 °C & stir the mixture for 1 h at 75-80 °C.		Clear solution is observed

20.	Then allow the clear solution to cool to 5-10 °C and maintain it at 5-10°C for 5 h.		Solid precipitate was observed
21.	Filter the solid and wash it with chilled (10-15 °C) water Lot-4.	0.7 L	
22.	Wash the solid with Acetone.	0.7 L	
23.	Dry the solid u/v at 50-55 °C for 3 h till constant weight.		
24.	Send the dried sample for analysis.		Purity by HPLC A% Result: A% 99.83, Assay: 99.4 w/w%
25.	Yield	760.0 g	Assay based yield: 60.53%

b) In process controls data:

S. No.	Batch Id	IPC-1 (Content of Compound-3)	Purity by HPLC
1	CR592-16492-32	Result: 0.92%	Attachment-12 EIDD-2801: 69.31%; Formyl IMP: 24.58%; NHC: 0.71%; SMI: 1.08%

After reflux with ethanol:

S. No.	Batch Id	IPC-2 (Content of EIDD-2801 & Impurity at 15.4/15.9 min)	HPLC Spectra
1	CR592-16492-32	Comp-3: 1.11%, EIDD-2801: 87.43%, Formyl IMP: 0.03%, 0.03%, NHC: 7.81%, Imp at RT 6.76 : 0.02%	Attachment-13

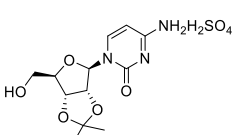
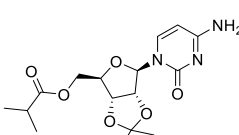
After 1st crystallization from water:

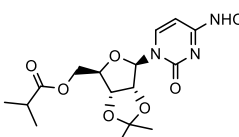
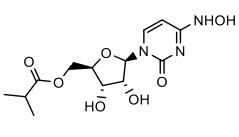
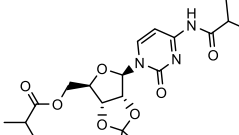
S. No.	Batch Id	IPC-3 (Content of EIDD-2801 & Impurity at 15.4/15.9 min)	HPLC-Spectra
1	CR592-16492-32	Comp-3: 0.46%, EIDD-2801: 98.62%, NHC: 0.83%,	Attachment-14

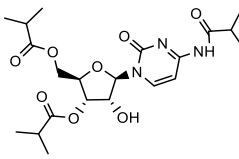
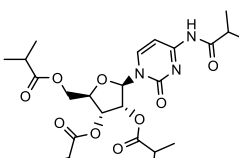
c) Results of the batch: After 2nd crystallization from water:

S. No	Batch No.	Input (kg)	Output (g)	Molar Yield (%)	Analytical data
1	CR592-16492-32	1.4	760.0	60.65	Attachment-15 HPLC A%: 99.83 HPLC w/w%: 99.4

Characterization Data of all compounds:

Structure/ Compound Code / Physical Nature	¹ H-NMR	¹³ C-NMR	LC-MS	HPLC
 Compound-1 Off-white solid Batch No.: CR592-16022-86-P	Attachment-16 (400 MHz, DMSO- <i>d</i> ₆): δ = 9.56 (s, 1H), 8.65 (s, 1H), 8.11 (d, <i>J</i> = 7.6 Hz, 1H), 6.13 (d, <i>J</i> = 8.0 Hz, 1H), 5.75 (s, 1H), 4.87 (d, <i>J</i> = 4.8 Hz, 1H), 4.72 (s, 1H), 4.21 (s, 1H), 3.62-3.41 (m, 2H), 1.44 (s, 3H), 1.25 (s, 3H).	Attachment-17 (100 MHz, DMSO- <i>d</i> ₆): δ = 159.3, 147.1, 145.4, 112.6, 93.6, 93.0, 87.8, 84.5, 80.5, 61.1, 26.9, 25.1.	Attachment-18 LCMS (M+H ⁺) calcd for C ₁₆ H ₂₄ N ₃ O ₆ : 283.4; Found: 284.0	Attachment-19 HPLC purity (RT 9.79 at 260.0 nm): 99.70%
 Compound-2 White crystalline solid Batch No.: CR592-16492-4-P1	Attachment-20 (400 MHz, D ₂ O): δ = 7.72 (d, <i>J</i> = 7.6 Hz, 1H), 6.03 (d, <i>J</i> = 7.2 Hz, 1H), 5.80 (s, 1H), 5.12-5.10 (m, 1H), 5.01-4.99 (m, 1H), 4.71 (s, 1H), 4.46-4.34 (m, 2H), 2.53-2.50 (m, 1H), 1.64 (s, 3H), 1.44 (s, 3H), 1.10 (t, <i>J</i> = 7.6 Hz, 6H)	Attachment-21 (100 MHz, DMSO- <i>d</i> ₆): δ = 175.7, 166.0, 154.7, 143.7, 112.7, 94.2, 94.0, 84.6, 84.1, 81.2, 64.2, 33.0, 26.8, 25.0, 18.6.	Attachment-22 LCMS (M+H ⁺) calcd for C ₁₆ H ₂₄ N ₃ O ₆ : 353.4; Found: 354.43.	Attachment-23 HPLC purity (RT 14.97 at 260.0 nm): 94.59%.

 <p>Compound-3</p> <p>White solid</p> <p>Batch No.: CR592-16492-26 -P</p>	<p>Attachment-24</p> <p>(400 MHz, DMSO-<i>d</i>₆): δ = 10.05 (s, 1H), 9.65 (s, 1H), 6.88 (d, <i>J</i> = 8.0 Hz, 1H), 5.71 (s, 1H), 5.56 (d, <i>J</i> = 8.0 Hz, 1H), 4.95-4.93 (m, 1H), 4.76-4.74 (m, 1H), 4.24-4.09 (m, 3H), 2.59-2.50 (m, 1H), 1.47 (s, 3H), 1.28 (s, 3H), 1.08 (d, <i>J</i> = 6.8 Hz, 6H)</p>	<p>Attachment-25</p> <p>(100 MHz, DMSO-<i>d</i>₆): δ = 175.8, 148.9, 143.1, 131.8, 113.29, 98.5, 91.1, 83.0, 80.5, 63.74, 32.98, 26.9, 25.0, 18.6.</p>	<p>Attachment-26</p> <p>LCMS (M+H⁺) calcd for C₁₆H₂₃N₃O₇: 369.4; Found: 369.7</p>	<p>Attachment-27</p> <p>HPLC purity (RT:19.23 at 260.0nm): 98.70%</p>
 <p>MK-4482/EIDD-2801/Molnupiravir</p> <p>White Crystalline solid</p> <p>Batch No.: CR592-15288-53</p>	<p>Attachment-28</p> <p>(400 MHz, MeOD): δ = 6.89 (d, <i>J</i> = 8.4 Hz, 1H), 5.80 (d, <i>J</i> = 4.8 Hz, 1H), 5.60 (d, <i>J</i> = 8.4 Hz, 1H), 4.28 (d, <i>J</i> = 3.6 Hz, 2H), 4.12 (t, <i>J</i> = 4.8 Hz, 1H), 4.09-4.05 (m, 2H), 2.64-2.57 (m, 1H), 1.16 (d, <i>J</i> = 7.2 Hz, 6H),</p>	<p>Attachment-29</p> <p>(100 MHz, MeOD): δ = 178.4, 151.6, 146.2, 131.8, 99.6, 90.5, 82.7, 74.5, 71.6, 65.0, 35.2, 19.49, 19.45.</p>	<p>Attachment-30</p> <p>LCMS (M+H⁺) calcd for C₁₃H₁₉N₃O₇: 329.3 Found:330.23</p>	<p>Attachment-31</p> <p>HPLC purity (RT:13.69 at 260.0nm): 99.67%</p>
 <p>White solid (Di-acyl)</p> <p>Stage-2 impurity</p> <p>Batch No.: CR592-15306-63 -Diacyl</p>	<p>Attachment-32</p> <p>(400 MHz, DMSO-<i>d</i>₆): δ = 10.9 (s, 1H), 8.11 (d, <i>J</i> = 7.6 Hz, 1H), 7.22 (d, <i>J</i> = 7.2 Hz, 1H), 5.79 (s, 1H), 5.01 (d, <i>J</i> = 5.2 Hz, 1H), 4.82 (s, 1H), 4.33-4.18 (m, 3H), 2.73-2.69 (m, 1H), 2.49-2.45 (m, 1H), 1.48 (s, 3H), 1.29 (s, 3H), 1.06-1.02 (m, 12H)</p>	<p>Attachment-33</p> <p>(100 MHz, DMSO-<i>d</i>₆): δ = 177.7, 175.6, 163.1, 154.2, 147.2, 112.7, 95.3, 94.8, 85.1, 84.3, 80.9, 63.9, 34.7, 32.9, 26.7, 24.9, 18.8, 18.7, 18.5, 18.4.</p>	<p>Attachment-34</p> <p>LCMS (M+H⁺) calcd for C₁₃H₁₉N₃O₇: 423.2 Found: 424.16</p>	<p>Attachment-35</p> <p>HPLC purity (RT:22.11 at 260.0nm): 99.25%</p>

 <p>White solid (tri-acyl) Stage-2 impurity Batch No.: CR592-15288-58-Triacyl</p>	<p><u>Attachment-36</u> (400 MHz, DMSO-<i>d</i>₆); δ = 7.61(d, <i>J</i> = 7.2 Hz, 1H), 7.31 (d, <i>J</i> = 8.0 Hz, 2H), 5.82 (d, <i>J</i> = 4.4 Hz, 1H), 5.75 (d, <i>J</i> = 7.6 Hz, 1H), 5.44-5.41 (m, 1H), 5.37-5.35 (m, 1H), 4.30-4.21 (m, 3H), 2.61-2.49 (m, 3H), 1.11-1.06 (m, 18H).</p>	<p><u>Attachment-37</u> (100 MHz, DMSO-<i>d</i>₆): δ = 175.6, 174.88, 174.84, 165.7, 154.6, 142.2, 94.6, 89.5, 78.7, 72.4, 69.8, 63.0, 33.0, 32.9, 18.6, 18.56, 18.51, 18.46, 18.40</p>	<p><u>Attachment-38</u> LCMS (M+H⁺) calcd for C₁₃H₁₉N₃O₇: 453.5 Found:454.46</p>	<p><u>Attachment-39</u> HPLC purity (RT:22.11 at 260.0nm): 99.25%</p>
 <p>White solid (Tetra-acyl) Stage-2 impurity Batch No.: CR592-15288-58-F1-(tetra acyl)</p>	<p><u>Attachment-40</u> (400 MHz, MeOD): δ = 8.11 (d, <i>J</i> = 7.2 Hz, 1H), 7.50 (d, <i>J</i> = 7.6 Hz, 1H), 6.00 (s, 1H), 5.53-5.51 (m, 1H), 5.38 (t, <i>J</i> = 5.6 Hz, 1H), 4.44-4.35 (m, 3H), 2.71-2.56 (m, 4H), 1.19-1.15 (m, 24H),</p>	<p><u>Attachment-41</u> (100 MHz, MeOD): δ = 178.8, 176.9, 176.0, 175.9, 164.0, 156.6, 145.2, 97.4, 90.7, 80.6, 74.1, 70.2, 62.9, 36.2, 34.1, 34.0, 18.4, 18.3, 18.28, 18.23, 18.1</p>	<p><u>Attachment-42</u> LCMS (M+H⁺) calcd for C₁₃H₁₉N₃O₇: 523.6 Found:524.1</p>	<p><u>Attachment-43</u> HPLC purity (RT:22.11 at 260.0nm): 99.25%</p>

Analytical Procedure

Chromatographic purity by HPLC:

Chemicals / Reagent references:

- a) Ortho phosphoric acid
- b) Acetonitrile
- c) Milli-Q water

A) Preparation of Mobile Phase:

Mobile Phase A : 0.1% Ortho phosphoric acid in water.

Mobile Phase B : Acetonitrile : Water (90 : 10)

Diluent : Water (For compound-1, compound-3, compound-4)
Water:Acetonitrile::90:10 (Compound-2)

B) Chromatographic conditions:

Column : XTerra RP-18, (250 x 4.6mm), 5 μ
 Detector Wavelength : 260 nm
 Flow rate : 1.0 ml/min.
 Injection Volume : 10 μ l
 Run Time : 40 minutes
 Column Temp : 35°C

C) Gradient Program:

S.No.	TIME (in mins)	Mobile Phase A	Mobile Phase B
1	0.0	98	02
2	5.0	98	02
3	25.0	20	80
4	30.0	20	80
5	31.0	98	02
6	40.0	98	02

D) Preparation of solutions:

Blank Solution : Diluent

Test solution:

Accurately weigh and transfer 25.0 mg of sample into the 50 ml volumetric flask add about 30ml of diluent, sonicate and make up the volume to 50 ml with diluent (Concentration is about 500 ppm).

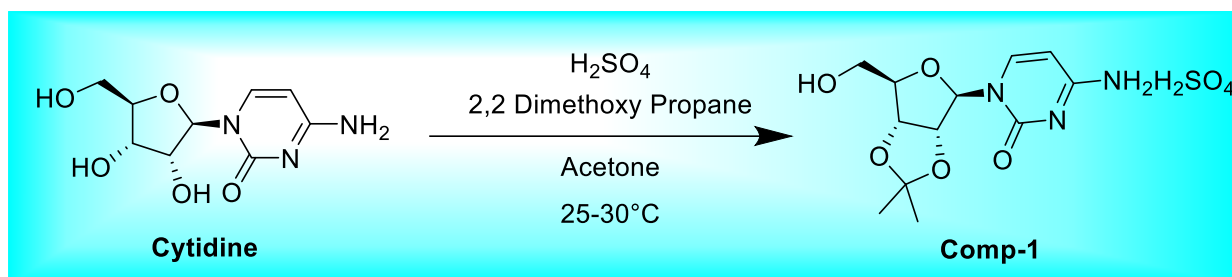
Integrate the chromatograms appropriately by are normalization method.

Retention time of known SM, intermediates and Final compound

Sl. No.	Compound	Retention time (min)
1.	Cytidine	2.8
2.	Uridine	4.4
3.	NHC	3.4
4.	Compound-1	9.8
5.	Compound-2	15.45
6.	Di-acyl stage-2 impurity	22.1
7.	Compound-3	19.25
8.	EIDD-2801	13.8
9.	Uridine-acyl impurity	14.7
10.	Cytidine-acyl impurity	11.8

Results and discussion

Optimization of Step-1:



Protocol:

To the dry acetone (10 V), charged 2,2-dimethoxypropane (DMP) and cytidine (KSM) (1.0 eq) at 25-30 °C under nitrogen atmosphere, then cooled to 10-15 °C and slowly added conc. H₂SO₄ at 10-15 °C. After complete addition of H₂SO₄ temperature was slowly raised to 25-30 °C and maintained for 14 h under nitrogen. Filtered the reaction mass, washed with acetone (10 V) and followed by slurry washed with MTBE (5 V). Solid was dried under vacuum at 45-50 °C.

Comparative data:

Reagent equivalent optimization

S.No	Batch No	Input Cytidine (g)	DMP (eq)	Acid (eq)	Output (g)/ Yield (%)	Analytical data	Remarks
1	CR592-15288-38	100.0	5.0	H ₂ SO ₄ (2.4)	154.65/ 98.65	Purity: 99.68% (by HPLC),	
2	CR592-16022-28	100.0	2.5	H ₂ SO ₄ (1.5)	153.2/ 97.79	Purity: 99.39% (by HPLC), SM: 0.15%,	
3	CR592-16022-31	10.0	2.5	H ₂ SO ₄ (0.5)	--	Purity: 44.47% (by HPLC), SM: 55.33%,	Not purified
4	CR592-16022-42	10.0	5.02	PTSA (2.4)	18.6/ 86.98	IPC: Cytidine (SM): 88.74%, Comp-1: 7.08	
5	CR592-15288-63	10.0	5.02	CSA (2.4)	--	SM : ~65%, NHC: ~12%, SMI: ~15% Comp-1: (BDL)	

6 √	CR592-16022-38	200.0	1.2	H ₂ SO ₄ (1.2)	306.5 g (97.7%)	Purity: 99.32% (by HPLC), SM: 0.18%,	
7 √	CR592-16022-86	1000.0	1.2	H ₂ SO ₄ (1.2)	1.58 Kg Assay based yield: 97.27%	HPLC: 99.70% SM: 0.28%	

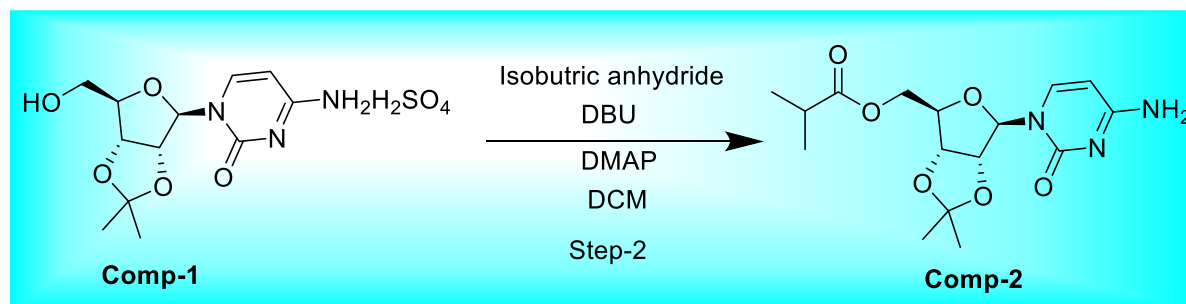
Solvent and reagent screening:

S.No	Batch No	Input Cytidine (g)	DMP (eq)	Acid (eq)	Output/ Yield (%)	Analytical data	Remarks
Used 2-Me THF instead of Acetone:							
1	CR592-16022-34	10.0	2.5	H ₂ SO ₄ (1.5)	15.1/ 97.79	Purity: 98.68% (by HPLC), SM: 1.06%	2-MeTHF and acetone have similar reaction profile but acetone is more favorable as cost effective.
Reaction in 2-Me THF instead of Acetone and used PTSA as acid :							
2	CR592-16022-35	10.0	2.5	PTSA (1.5)	--	Purity: 65.07% (by HPLC), SM: 29.85%	In-complete conversion

Potential impurities and their origin:

In compound-1: Un-reacted SM Cytidine was observed as a major impurity.

Optimization of Step-2:



Protocol:

To the DCM (10 V), added comp-1 (1.0 eq), DMAP and DBU at 25-30 °C. RM was stirred for 10-15 min and cooled to 0 ± 5 °C and added isobutyric anhydride and maintained for 4 h at 0 ± 5 °C. Checked the consumption of Comp-1 by HPLC. Added cold 10% acetic acid solution (10V at 10-15 °C) and layers were separated. Organic layer was washed with cold 10% saturated sodium bi carbonate solution (2 X 5V at 10-15 °C). Then dried over anhydrous sodium sulphate and distilled completely at 40-45 °C, solid compound was obtained. Crude was unloaded and charged n-hexane (5V) with continuous stirring at 25-30 °C for 30 min to make the solid free. Next free solid was filtered u/N2 and dried u/v below 35 °C.

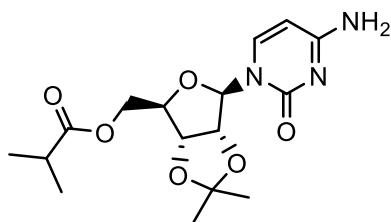
Comparative data:

S.No	Batch No	Input Comp-1 (g)	Solvent (V)	Iso butyric anhydride (eq)	DBU (eq)	DMAP (eq)	Output (g)/ Yield (%)	Analytical data
1	CR592-15288-44	50.0	ACN	1.1	2.1	0.2	45.0	Comp-2: 89.37%, comp-1: -BDL, Di-acyl: 8.61%, SMI: 0.77
2	CR592-15288-47	2.0	Toluene	1.1	2.1	0.2	-	Comp-2: 70.59%, comp-1: -BDL, Di-acyl: 22.33%
3	CR592-15306-31	2.0	DCM	1.1	2.1	0.2	-	comp-2: 97.87, Di-acyl: 1.55%, SMI: 0.26 %
4	CR592-15306-30	10.0	DCM	0.9	2.1	0.2	-	Comp-2: 80.17%, comp-1: 15.90, Di-acyl: 2.52%
5	CR592-15365-22	10.0	DCM	1.1	2.1	0.0	-	Comp-2: 76.65%, comp-1: 4.82, Di-acyl: 16.51%
6	CR592-15365-23	10.0	DCM	1.1	0.0	2.1	-	Comp-2: 61.91%, comp-1: 8.59%, Di-acyl: 25.55%
7	CR592-15306-57	140.0	DCM	1.1	2.1	0.2	123.5 g / 95.21	Comp-2: 94.17%, Di-acyl: 1.28%,
<p>The reaction was optimized on 140.0 g scale using 10 V of DCM, 1.1 eq of Iso butyric anhydride, 2.1 eq of DBU & 0.2 eq of DMAP. Hence, further it was scaled up to 1.0 Kg scale and the results are shown below.</p>								
8√	CR592-16492-8	1000	DCM	1.1	2.1	0.2	881.87/ 87.03	comp-2: 93.83%; di-acyl: 5.15%

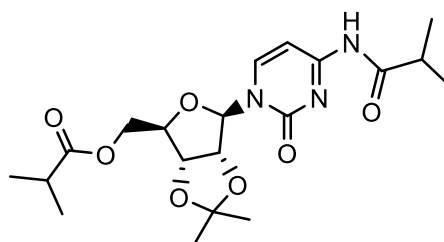
							Assay based yield	Attachment-5
--	--	--	--	--	--	--	-------------------	------------------------------

* BDL: Below detection limit

Structures of Impurity & comp-2:



Molecular Weight: 353.38
Comp-2



Molecular Weight: 423.47
Di-acyl Comp-2 impurity

Efforts were directed towards the direction of conversion of the Stage-2 di-acyl impurity to Compound-2 as well as purification of compound-2 to eliminate the di-acyl impurity.

Several solvents were checked for the crystallization or trituration of crude compound-2 to purge di-acyl impurity but without success.

Next, compound-2-di-acyl impurity was treated with aq. NH₂OH and it was observed that most of the di-acyl impurity was converting towards the compound-2.

Details are shown below.

Synthesis of Compound-2:

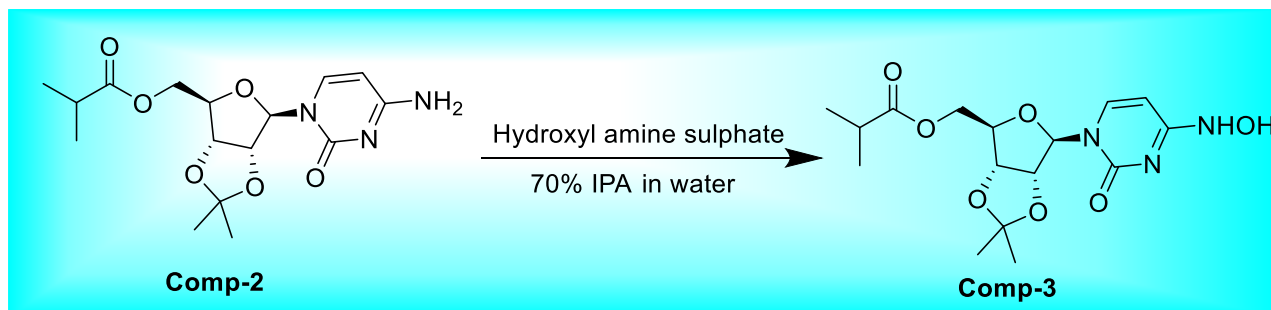
S.No	Batch No	Input Comp-1 (g)	Solvent (V)	Iso butyric anhydride (eq)	DBU (eq)	DMAP (eq)	Output (g)/ Yield (%)	Analytical data
1	CR592-16022-89	1500	DCM	1.1	2.1	0.2	1287.2 g	Comp-2:-88.95%, comp-1 (BDL), Di-acyl:-10.11% Attachment-44

In this batch during work up temperature was higher 20-25°C than usual 0-10°C, and Di-acyl was observed ~10%.

Next, this material was treated with 50% aq. NH₂OH in DCM at 25-30°C for 5h and layers were separated. DCM layer was washed with 5V water and dried over anhydrous. Na₂SO₄ and evaporated under reduced pressure to afford the Crude Compound-2 which was used as such in next step.

S.No	Batch No	Input Comp-2 (g)	Solvent (V)	50% NH ₂ OH	Output (g)/ Yield (%)	Analytical data
1	CR592-16492-21	500 CR592-16022-89	DCM 5	140.0 g 18 eq of Di-acyl impurity	500.0 g	Comp-2:-97.67%, Di-acyl;--BDL Attachment-45

Optimization of Step-3:



Optimization of step-3 by modified workup:

Batch No	Input Comp-2	Protocol	Remark/Analytical data

CR592-15288-34	5.0 g	<p>General protocol: Comp-2 (5.0 g) was added to 70% Aqueous IPA (10V) and slowly charged Hydroxylamine sulphate (3.2eq) and RM heated to 75-80°C and maintained for 16 h.</p> <p>Work-up: - RM distilled completely added 10vol of Acetonitrile and stirred for 30min. Filtered salts and filtrate distilled. Added (10V) toluene and distilled toluene. Cooled to 10-15°C and filtered.</p>	Crude:- Comp-3: 74.20%, comp-2: 2.27%, MK-4482(EIDD-2801): 5.11 NHC: 14.43
CR592-15365-27	85.0 g	<p>Modified workup protocol: Comp-2 (5.0g 1.0eq) was added to 70% Aqueous IPA (10V) and slowly charged Hydroxylamine sulfate (3.2eq) and RM heated to 75-80°C and maintained for 16 h. Cooled RM to 25-30°C</p> <p>Workup: - Layers separated and IPA layer distilled off U/V at 40-45°C. Added (10V) of Isopropyl acetate and (5V) of H₂O, taken organic layer and washed with (5V) of sat. NaCl solution then distilled. Solid crude compound obtained</p>	Crude: Comp-3: 89.32%, comp-2: 0.14%, MK-4482(EIDD-2801): 6.70% SMI: 2.21%
Remarks: Instead of removing all the aqueous solvent by distillation, simple layer separation provided better quality compound-3			

Optimization of step-3 using hydroxylamine sulphate (0.61 eq) in 70:30 (IPA:H₂O)

General protocol: - Comp-2 (10.0 g) was added to 70% IPA in water (10V) and slowly charged Hydroxylamine sulphate (1.5 eq) and RM heated to 75-80 °C and maintained for 14 h.

Batch No	Solvent	Input (Comp-2)	Remark/Analytical data	
			IPC-14h	IPC-18h
CR592-16492-11	70:30 (IPA:H ₂ O)	10.0 g	comp-2: 19.43% comp-3: 63.40%, MK-4482: 8.35%,	comp-2: 10.96% comp-3: 57.93%, MK-4482: 17.38%,

Observation: - Using 0.61 eq of (NH₂OH)₂SO₄ incomplete conversion of SM as well as considerable amount of MK-4482 formation was observed.

Optimization of step-3 by using 1.5 equivalent of Hydroxyl amine sulphate in different solvent:

General protocol: - Comp-2 (10.0 g) was added to IPA in water (10V) and slowly charged Hydroxylamine sulphate (1.5 eq) and RM heated to 75-80 °C and maintained for 14 h.

Batch No	Solvent	Input (Comp-2)	Remark/Analytical data
CR592-16022-77	H ₂ O	10 g	Comp-2:-0.05%, <u>Comp-3:0.13%</u> , EIDD:-29.26%, Uridine:31.25%, Cytidine:8.73%, Uridine acrylated:24.97%, Cytidine acylated:5.03%, Observation: Comp-3 formation was very less and more impurities were observed.
CR592-16022-78	30:70 (IPA:H ₂ O)	10 g	Comp-2:-BDL%, <u>Comp-3:BDL%</u> , EIDD:-51.41%, Uridine:15.69%, Cytidine:3.14%, Uridine acrylated:26.28%, Cytidine acylated:2.80%, Observation: In this condition Comp-3 was not observed, and more impurities were formed.
CR592-16022-79	50:50 (IPA:H ₂ O)	10g	Comp-2:-BDL%, Comp-3: 3.47%, <u>EIDD:74.14%</u> , Uridine:3.54%, Cytidine:0.93%, <u>Uridine acylated:15.01%</u> ,Cytidine acylated:1.75%, Observation: In this condition compare to comp-3, MK-4482 was formed more and higher uridine acylated impurity formed
CR592-16022-80	70:30 (IPA:H ₂ O)	10g	Comp-2: 2.18%, Comp-3: 87.57%, EIDD: 6.41%, Uridine:31.25%, Cytidine:8.73%, Uridine acrylated:24.97%, Cytidine acylated:0.35%, Observation: Obtained best results in this conditions among all the screened condition and same condition was used for scale up.

Scale up data using 70:30 (IPA:H₂O) condition:

Batch No	Solvent	Input (Comp-2)	Remark/Analytical data
CR592-16492-18	70:30 (IPA:H ₂ O)	100 g	IPC-1 (12h): comp-2: 2.70% comp-3: 83.40%, MK-4482: 9.29%, IPC-2 (18h): comp-2: 2.02% comp-3: 73.25%, MK-4482: 16.73%,

Observation: Under this condition reaction conversion was good but after extended stirring compound-3 was converted to MK-4482 and other un-known impurities.

Optimization of step-3: using Hydroxyl amine sulphate (1.5 eq) and 0.12 eq of DMAP

General protocol: Comp-2 (1.0 eq) was added to 70% Aqueous IPA (10 V) and added DMAP (0.12 eq) slowly charged Hydroxylamine sulfate (1.5 eq) and RM heated to 75-80 °C and maintained for 28 h. Cooled RM to 25-30 °C. Separated the layers. Organic layer distilled off u/v below 45 °C. Crude dissolved in IPAc (10 V) and washed with water (5 V) followed by aq. NaCl sol. (15%, 5 V). Organic layer distilled off to ~2.5 V and cooled to 10-15 °C (crystallization starts ~40-45 °C) and aged for 8 h and filtered and washed with 0.5 V IPAc and dried at 45-50 °C in ATD till constant weight (~8 h).

Batch No	Input (Comp-2)	Output (% yield)	Analysis data	
			IPC-14 h	IPC-20 h
CR592-16492-19	50.0 g	35.1 g/ 68.15	comp-2: 3.49% comp-3: 88.08%, MK-4482: 4.29%,	comp-2: 3.50% comp-3: 87.77%, MK-4482: 4.39%

Observation: DMAP played a crucial role to prevent the hydrolysis of Comp-3 to MK-4482 and extended time of heating was also tolerated efficiently. Next, we checked the effect of different organic bases and results are summarized below.

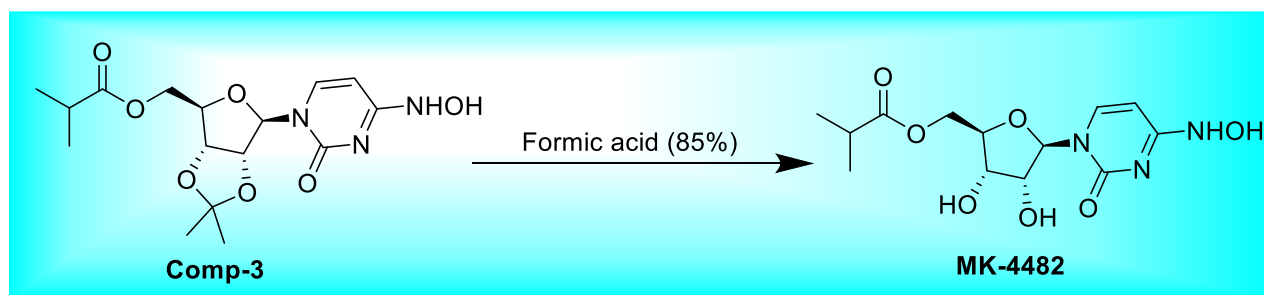
Batch No	Input SM (Stage-2)	0.12 eq Base	Remark/Analytical data		
			6h IPC	12h IPC	24h IPC
✓ CR592-16492-19	CR592-16492-8 Comp-2:- 93.83% Di-acyl:- 5.15%, SMI :- 0.20 % Assay: 88.9%	DMAP pKa: 9.6 (H ₂ O)		comp-2: 3.49% comp-3: 88.08%, MK-4482: 4.29%,	comp-2: 3.50% comp-3: 87.77%, MK-4482: 4.39%,
CR592-16492-33		TEA pKa: 10.75 (H ₂ O)	comp-2: 13.84%, comp-3: 80.75%, MK-4482: 1.90%,	comp-2: 0.36%, comp-3: 88.30%, MK-4482: 8.11%	comp-2: 0.07%, comp-3: 80.80%, MK-4482: 14.52%,
CR592-16492-34		Pyridine pKa: 5.5	comp-2: 14.31%, comp-3: 80.12%, MK-4482: 2.04%,	comp-2: 0.66%, comp-3: 87.56%, MK-4482: 8.70%,	comp-2: 0.16%, comp-3: 83.31%, MK-4482: 12.54%,
CR592-16511-15		DIPEA pKa: 10.75	comp-2: 69.32%, comp-3: 30.18%, MK-4482: NA- %,	comp-2: 0.33%, comp-3: 93.12%, MK-4482: 3.82%,	comp-2: 0.05%, comp-3: 88.92%, MK-4482: 7.88%,
✓		N-Methyl Imidazole pKa: 7.06	comp-2: 43.84%, comp-3: 55.37%,	comp-2: 13.96%, comp-3: 84.34%, MK-4482: 0.48%,	comp-2: 1.27%, comp-3: 94.75%, MK-4482: 1.66%,

CR592-16511-17			MK-4482: 0.04%		
Remark: Both N-Methylimidazole, and DMAP were found to be effective for the conversion of comp-2 to compound-3 with minimum MK-4482 formation					

Scale up using catalytic DMAP and 1.5 eq of Hydroxylamine sulfate:

Batch No	Input	Output	Remark/Analytical data		
			IPC	Crude	Pure
CR592-16492-25	500 g	367.5 g/ 70.1	comp-2: 1.81%, comp-3: 92.65%, MK-4482: 3.04%	comp-2: 0.49%, comp-3: 93.30%, MK-4482: 2.46%	comp-3: 99.13%, MK-4482: 0.74%, SMI: 0.13% Attachment-10
CR592-16492-26	1.0 Kg	740 g/ 69.2	comp-2: 2.69%, comp-3: 90.15%, MK-4482: 4.51%	comp-2: 0.50%, comp-3: 93.72%, MK-4482: 2.55%	comp-3: 98.70%, MK-4482: 1.06%, SMI: 0.19%

Optimization of Step-4:



Optimization of Stage-4 reaction conditions by using various acidic reagents & volume

Batch No	Input Comp-3	Reagent	Protocol	Remark/Analytical data

Comp-3

CR592-15365-29	5.0 g	Formic acid (85%)/16V	General protocol: To the Comp-3 added 85% HCOOH and stirred for 6hr's at 25-30 °C. Distilled completely U/V at 45-50°C and Co-distilled with ethanol (6V) u/v at 40-45°C.	IPC: Comp-4: 90.26%, comp-3: 1.16%, SMI: 4.78%
CR592-15365-30	5.0 g	Formic acid (98%)/16V	To the Comp-3 added 98% HCOOH and stirred for 6hr's at 25-30 °C. Distilled completely U/V at 45-50°C and Co-distilled with ethanol (6V) u/v at 40-45°C.	IPC: Comp-4: 53.78%, comp-3: 42.19%, SMI: 2.21%
CR592-15365-31	5.0 g	Acetic acid (70%)/16V	To the Comp-3 added 70% CH ₃ COOH and stirred for 24 h at 25-30°C. Distilled completely U/V at 45-50°C and Co-distilled with ethanol (6V) u/v at 40-45°C.	IPC: Comp-4: 17.50%, comp-3: 81.41%, SMI: 0.53%
CR592-15365-33	1.0 g	Amberlyst(R) 15 hydrogen form /H ₂ O (10 V)	To the Comp-3 added AmberlystI-15-H ⁺ and stirred for 24 h at 25-30°C. Distilled completely U/V at 45-50°C and Co-distilled with ethanol (6V) u/v at 40-45°C.	IPC: Comp-4: 64.21%, comp-3: 20.32%, SMI: 15%
CR592-15306-44	10.0 g	Amberlyst/ACN (10 V)	To the Comp-3 added Amberlyst/ACN and stirred for 24 h at 25-30°C. Distilled completely U/V at 45-50°C and Co-distilled with ethanol (6V) u/v at 40-45°C.	IPC: Comp-4: 46.83%, comp-3: 26.23%, SMI: 26.39%
CR592-16036-58	10.0 g	1M H ₂ SO ₄ in methanol	To the Comp-3 (10.0g), added 1M Sulphuric acid and stirred for 16h at 25-30 °C. Distilled completely U/V at 40-45°C and Charged	IPC: Comp-4: 46.83%, comp-3: 26.23%, SMI: 26.39%

			Ethanol (10V) and distilled u/v at 40-45°C. Gummy sticky mass observed. Hexane added and distilled off to get free solid.
Remarks: 85% HCOOH was provided better result and it was chosen for further optimization			

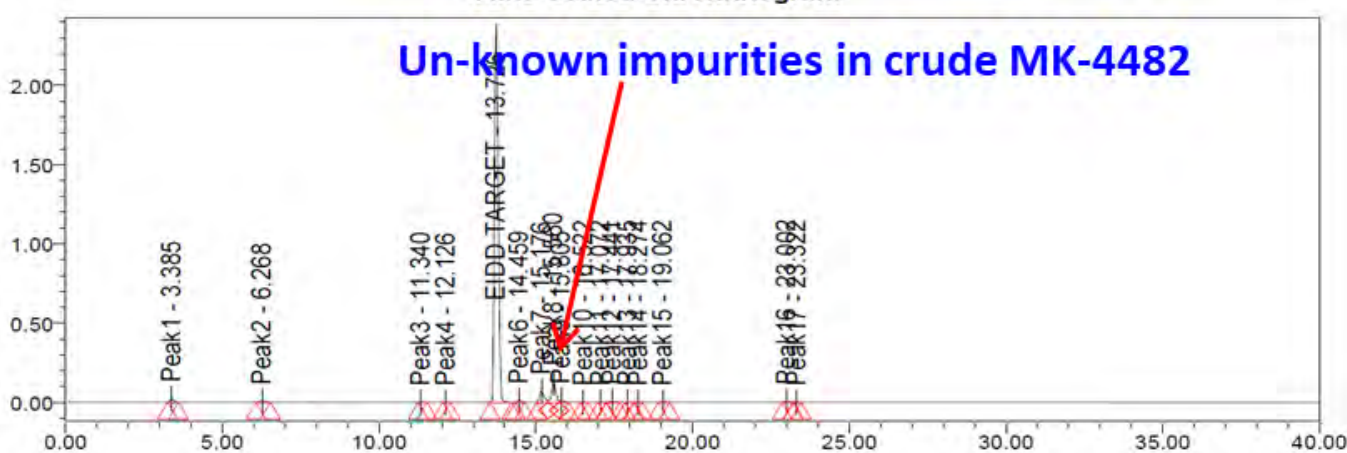
Optimization of volume of 85% Formic acid:-

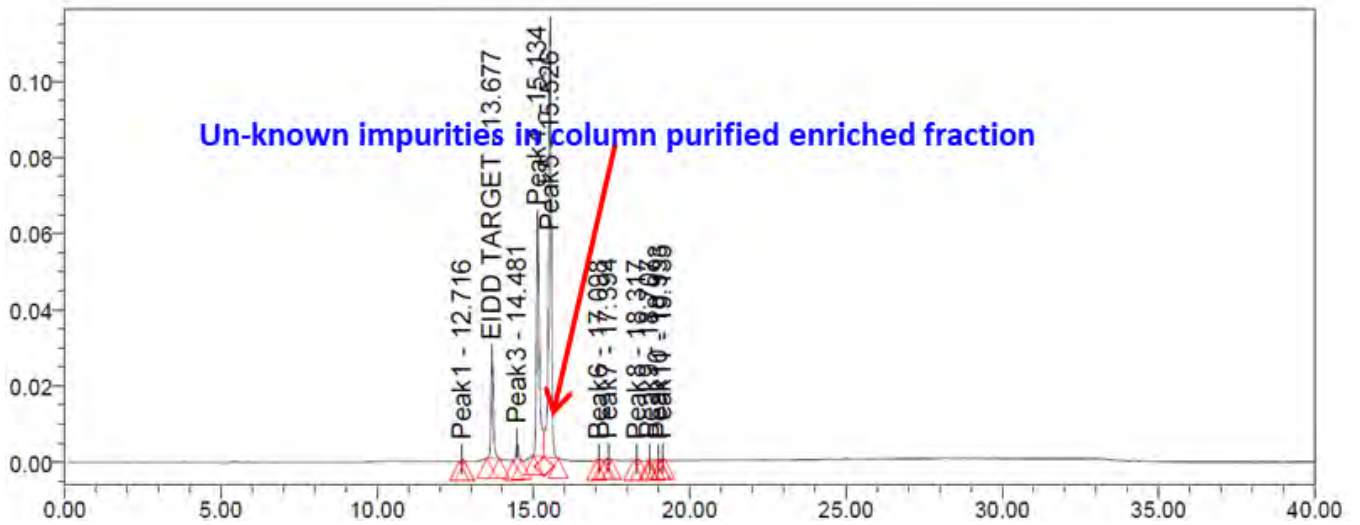
Batch No	Input Comp-3	Volume of 85%HCOOH	Area% of Compound-3 by HPLC
CR592-16306-74	10 g	10	IPC: Compound-3: 0.71%
CR592-16306-84	50 g	5	IPC :-Compound-3: 0.53

As the reaction went well, it was used in the scale up batch.

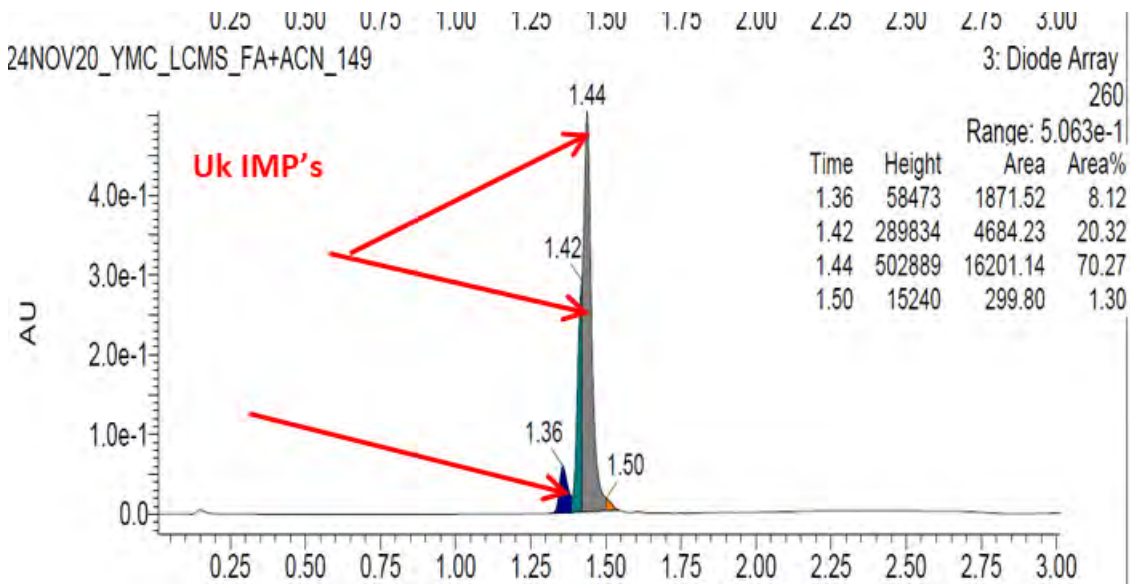
In this reaction couple of peaks were observed around 15.2-15.8 min region which were converted to MK-4482 while treating with Ethanol at elevated temperature. From one of the batch crude after treating with formic acid was isolated via column chromatography which showed highly enriched intermediate (15.2-15.8 min) region. That sample was subject to LCMS and 1HNMR analysis. From the result it can be predicted that those compounds most probably O-formates which on treatment with ethanol converts to MK-4482.

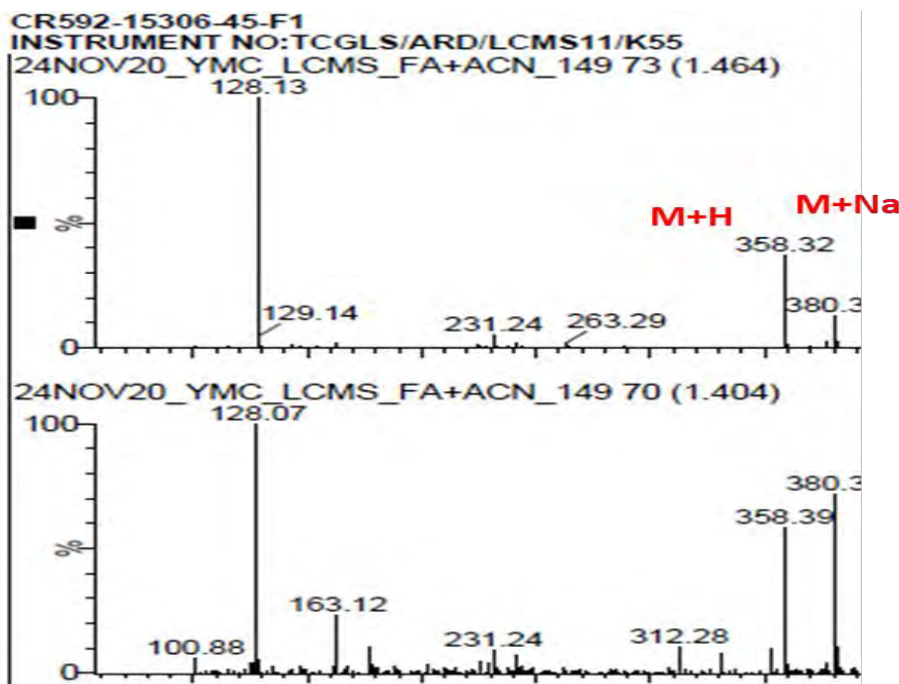
Data are shown below:



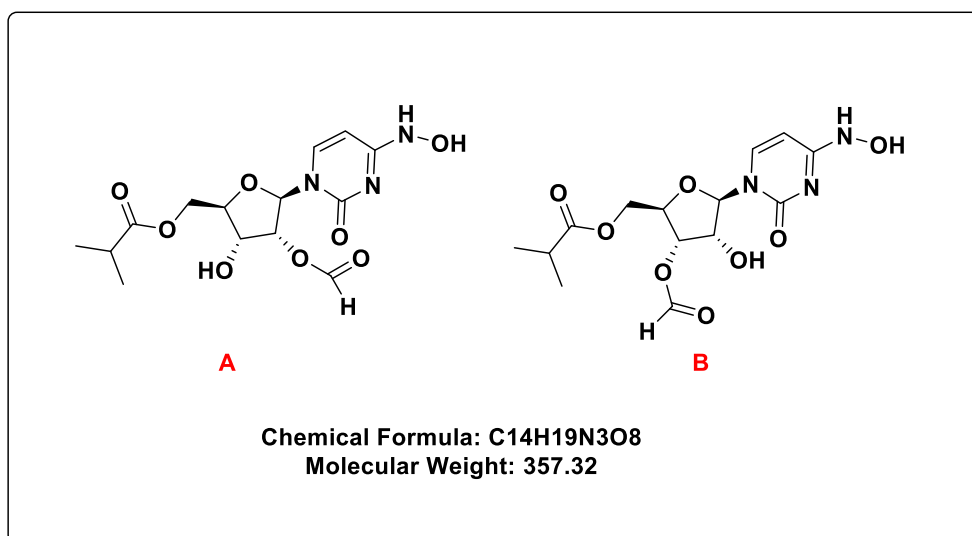


LCMS of the impurity enriched fraction:





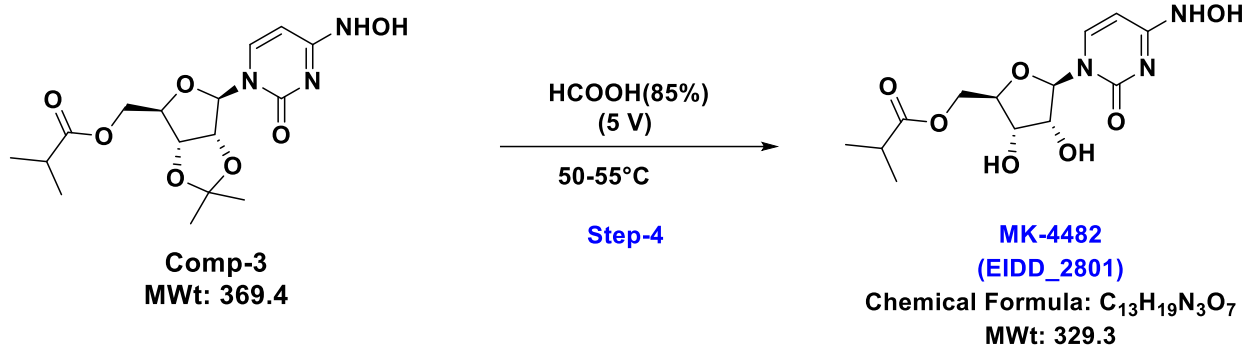
Probable structure of intermediates visible 15.2-15.8 min region:



In an effort to optimize the conversion of the formyl impurities to MK-4482, reaction was monitored for the conversion of the same while heating the reaction mass with ethanol.

[Attachment-46 \(1H NMR\)](#)

One representative example is shown below:



To the Comp-3 (50.0g), added 85% HCOOH (4V) and stirred for 6-8h at 50-55 °C, Distilled completely U/V at 40-45°C.

Batch No	Input SM (Comp-3)	Output/Yield (%)	Remark/Analytical data
CR592-16306-85	50.0g (CR592-16306-69)	Crude: 60.0 g NHC: 0.74 SM: 0.91 EIDD: 80.1 Formyl imp: 3.8/6.8/4.27	IPC: SM: 2.46 EIDD: 87.13 Formyl imp: 2.2/3.9

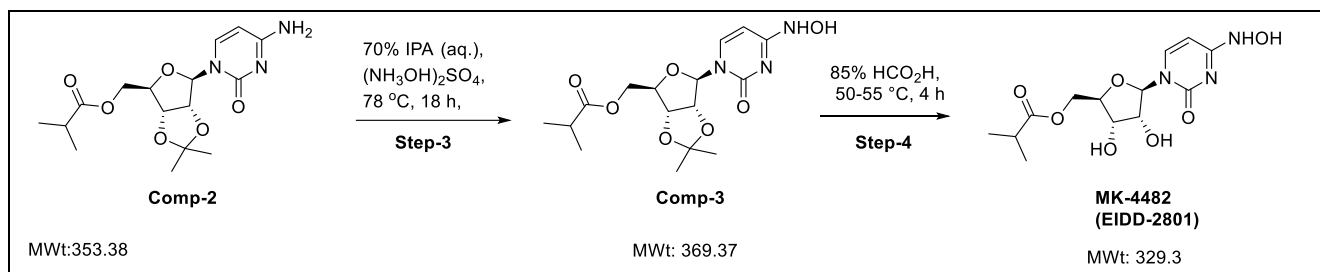
To the crude MK-4482/EIDD-2801, added ethanol and stirred for 24 h at reflux and progress of the reaction was monitored by HPLC.

Batch No	Crude	3h Reflux	6h Reflux	24h Reflux
CR592-16036-85	Crude:- NHC:0.74 SM-0.91 EIDD-80.1 Formyl imp-3.8/6.8/4.27 Attachment-47	NHC : 0.96 SM-1.1 EIDD-87.91 Formyl imp-2.7/4.9/0.14	NHC: 1.2 SM-1.0 EIDD-90.25 Formyl imp-1.8/3.2/0.11	NHC-2.1 SM-1.2 EIDD-93.9 Formyl imp-0.05/0.09/0.03 Attachment-48

Based on the above finding, scale up reaction was monitored for disappearance of the formyl impurities.

Telescoping of crude Compound-3 to MK-4482:

In view of product loss during purification of compound-3, the idea of taking forward the crude compound-3 to compound-4 (MK-4482/EIDD-2801/Molnupiravir) *via* telescoping mode was conceived and tested on reasonable scale. Results are summarized below.



Step-3:

Step No/ Batch No	Input (g)	Output (g)	Quality	Remark
3 CR592-16022-62	Compound-2 200.0 g CR592-16022-61	Compound-3 185.0 g	HPLC A%: Comp-3: 90.45% MK-4482: 2.88% SMI: 2.45% Attachment-49	Out of 185.0 g, 50.0 g was forwarded to next step

Step-4:

Step No/ Batch No	Input (g)	IPC after ethanol reflux	Remark
4 CR592-16036-84	Compound-3 50.0 g CR592-16022- 62-Crude	NHC: 2.81% Comp-3-0.39% EIDD-87.64% Formyl imp-0.15%, 0.49% Attachment-50	Crude weight 60.0 g

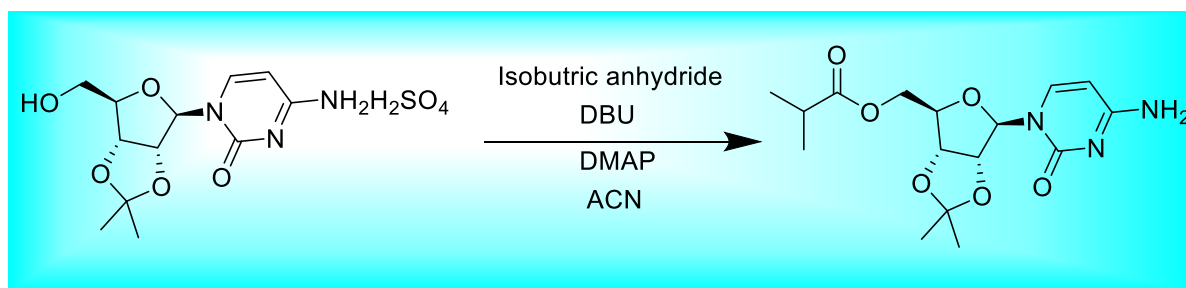
Purification of crude MK-4482:

Step No/ Batch No	Input (g)	Protocol	Yield (g)	Quality
4 CR592-16036- 84	Crude MK- 4482 60.0 g	Added 2 V of water to crude. Heated to 60-65 °C, and maintained 1h and gradually cooled to 25-30 °C and maintained for 16 h. Cooled to 10-15 °C and maintained for 3 h and filtered and washed with 2 X 0.5 V of chilled water.	30.0 g Yield from crude compound-3: 0.6 w/w	SM-0.18% EIDD-99.13% Formyl- 0.16/0.14% NHC: 0.36% Assay: 99.2% w/w

		Dried u/vacuum at 50-55 °C for 6 h.		
--	--	-------------------------------------	--	--

Above experiment clearly demonstrated that crude Compound-3 can be forwarded to next step without purification to afford similar quality material with better yield (**0.6 w/w** from crude compound-3). In case of purification, 523 g crude compound-3 afforded 367.5 g pure compound-3 (Batch No.: CR592-16492-25). Then 1.4 Kg pure compound-3 afforded 940 g (89.5% assay) MK-4482 after single water purification (CR592-16492-32). So overall w/w of MK-4482/crude compound-3 stands at **0.42 w/w**. This opens opportunity for further cost reduction keeping in mind the regulatory aspect.

Impurity profiling of Stage-2:

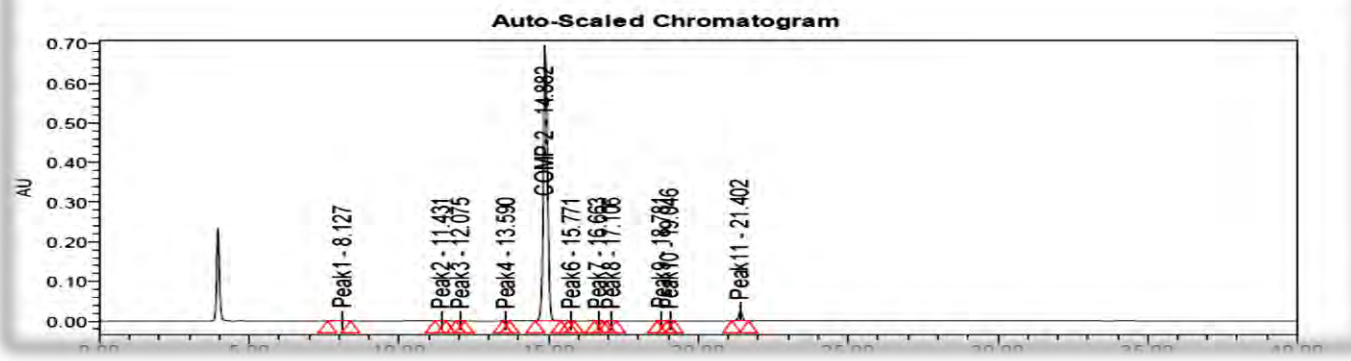


Batch No	Input Comp-2	Protocol	Remark/Analytical data
CR592-15306-33	250.0 g	To the DCM (10V), added comp-1(250.0g 1.0eq) DMAP (16.01g,0.204eq), and DBU (209.78g,2.1 eq) at 25-30°C RM cool to 0-5°C RM was stirred for 30min and added isobuteric anhydride (114.244mL,1.05eq) at 0-5°C over 45 min. *RM maintained for 4h at 0-5°C. Work up: Added water (10V) and washed with 10% Acetic acid (10V) and organic layer washed with saturated NaHCO ₃ (10V). organic layer Dried with anhydrous Sodium sulphate and distilled completely ,added hexane(10V) and stirred for 30min and filtered the compound to obtain the desired product as off-white colored solid	IPC-01: Comp-2 (96.20%), comp-1 (0.52%), SMI (2.91%) HPLC purity of Targeted comp: 95.99%, SMI: 3.54%, Yield: 210.70 g (~90%)

IPC-1:

SAMPLE INFORMATION

Sample Name:	CR562-15306-33-Rm-2[60mins]	Acquired By:	AM0113345
Sample Type:	Unknown	Sample Set Name:	TCGLS_111120
Vial:	53	Acq. Method Set:	EIDD_2801_OPA
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 260.0 nm (2998
Date Acquired:	11-11-2020 10:27:29 IST	Column Name:	XTERRA RP 18 (250X4.6)5u
Date Processed:	11-11-2020 11:16:52 IST		



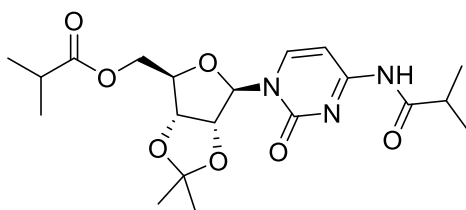
Peak Results

	Name	RT	Area	% Area	RT Ratio
1	Peak1	8.127	35503	0.52	0.546
2	Peak2	11.431	4685	0.07	0.768
3	Peak3	12.075	1668	0.02	0.811
4	Peak4	13.590	1469	0.02	0.913
5	COMP-2	14.882	6567384	96.20	1.000
6	Peak6	15.771	1136	0.02	1.060
7	Peak7	16.663	2386	0.03	1.120
8	Peak8	17.106	5140	0.08	1.149
9	Peak9	18.781	7990	0.12	1.262
10	Peak10	19.046	1380	0.02	1.280
11	Peak11	21.402	198395	2.91	1.438

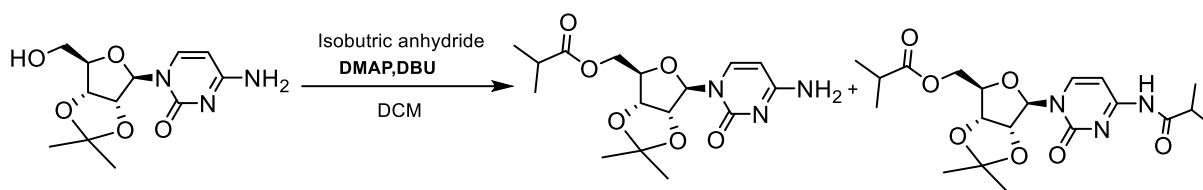
Impurity @ 21.402 min isolated by column chromatography and characterized by 1H & 13CNMR, LCMS.

It was further synthesized and RT was matched.

Di-acyl impurity Structure of the stage-2 is shown below



Molecular Weight: 423.47
Di-acyl impurity stage-2



Synthesis of the impurity @ 21.402 min

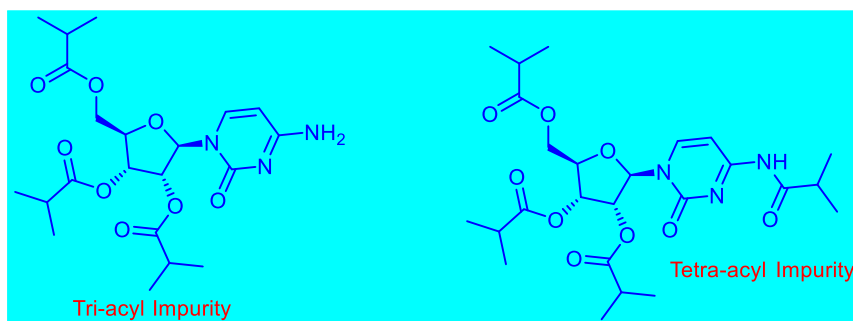
Protocol: To the DCM (10 V), added comp-1 (10.0 g), DMAP (0.204eq), and DBU (2.1eq) at 25-30 °C RM cool to 0-5 °C RM was stirred for 30 min and added isobutyric anhydride (1.05 eq) at 0-5 °C over 45 min. RM maintained for 4h at 0-5 °C.

Work up: Added water (10 V) and washed with 10% Acetic acid (10 V) and organic layer washed with saturated NaHCO₃ (10 V). Organic layer dried with anhydrous sodium sulphate and distilled completely, added hexane (10 V) and stirred for 30min and filtered the compound to obtain the desired product as off-white colored solid, and separated by column chromatography by using 20% ethyl acetate and hexanes. Yield = 2.0 g

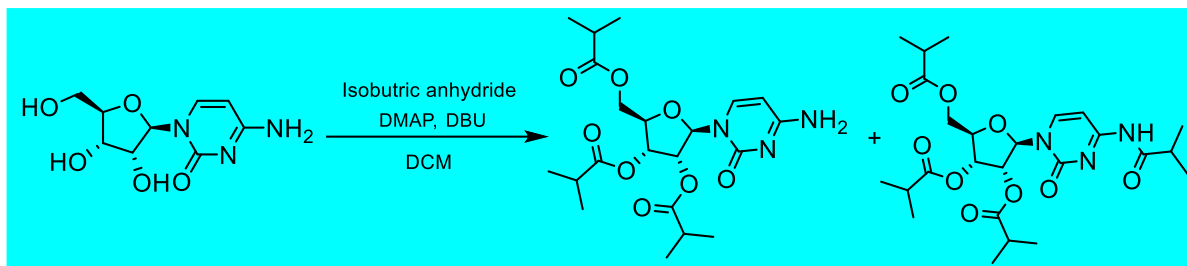
Batch No. CR592-15306-63:

Data analysis: [Attachments 32-35](#)

In few batches tri & tetra acyl impurity also observed at 19.29 RT & 25.89 RT, and this two impurities also prepared and characterized by LCMS 1H-NMR & 13C and data is shown below.



Synthesis of the Tri and tetra acyl impurities:-



Protocol: Arranged cleaned and dry RBF U/N₂ atm. charged cytidine and DCM at 25-30 °C and charged DBU & DMAP at 25-30 °C stirred for 15min and slowly charged isobutyric anhydride slowly at 25-30 °C maintained reaction overnight, then distilled completely DCM U/V at 40-45 °C and Charged (10 V) water and stirred for 15min and separated layers then taken org layer washed with (10 V) of 10% acetic acid and taken org layer washed with saturated NaHCO₃ solution. Taken organic layer and distilled DCM completely U/V at 40-45 °C, sticky solid observed then co-distilled with hexane (10V). White color free solid observed and this two impurities separated by column purification.

Batch No.: CR592-15288-58-(Triacyl)

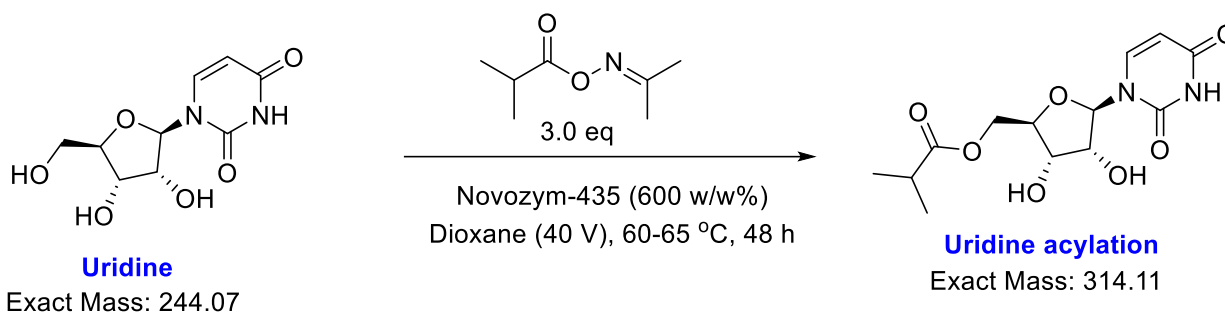
Data analysis: [Attachments 36-39](#)

Batch No.: CR592-15288-58-F1-(tetra acyl)

Data analysis: [Attachments 40-43](#)

Remark: This two impurities are also process impurities only and most probably formed due to presence of un-reacted isobutyric anhydride reacts with cytidine.

Uridine acylation (CR592-16036-37-F3):



Protocol:

To a suspension of uridine (2.0 g, 8.197 mmol) in 1,4-dioxane (80 V, 40 mL) was added oxime ester (3.5 g, 24.5 mmol), and Novozyme 435 (600 w/w%, 12.0 g). The reaction mixture was then stirred at 60 °C for 48 h. The mixture was then filtered to remove enzymes and washed with 1,4-dioxane (2 X 1 V). Then distilled 1, 4-dioxane and performed column chromatography.

Ref: *Macromolecules* **1999**, 32, 8725-8731.

¹H NMR: [Attachment-51](#)

HPLC: [Attachment-52](#)

LCMS: [Attachment-53](#)

Preliminary safety evaluation of isolated intermediates and Molnupiravir using DSC

DSC spectra of Compound-1: [Attachment-54](#)

Compound-1 showed decomposition from 183°C with liberation of heat 275 J/g

DSC spectra of Compound-2: [Attachment-55](#)

Compound-2 showed decomposition from 247°C with liberation of heat 320 J/g

DSC spectra of Compound-3: [Attachment-56](#)

Compound-3 melted at ~159°C and showed decomposition from 197°C with liberation of heat 60 J/g

DSC of Molnupiravir synthesized via chemical route: [Attachment-57](#)

Molnupiravir melted at ~155°C and showed decomposition from 222°C with liberation of heat 316 J/g

PSD data of MK-4482 (Molnupiravir)

[\(Attachment-58\)](#)

PXRD data of MK-4482 (Molnupiravir)

[Attachment-59](#)

Further areas of developments / improvements

Although the process has been scaled up to 1.4 Kg scale, there is still scope for further improvements:

- ❖ Step-1: Isolation and stability needs to be further optimization require
- ❖ Step-2: There is a scope to reduce the di-acyl impurity and purification to control carry-forward process un-identified impurities
- ❖ Step-3: Further studies of yield improvement, and control of impurity formation
- ❖ Step-4: Further exploration of crystallization to improve the isolated yield and better polymorph
- ❖ Telescoping of step-3 and step-4 without purifying compound-3 to reduce the cost

Acknowledgement: TCG would like to thank VCU to provide an opportunity to work on such a challenging development project. We would also like to thank Dr B. Frank Gupton, Dr. Dinesh J. Paymode, Dr. Ryan Nelson, and Dr, David Snead for the valuable comments, continuous guidance, encouragement to the team efforts and unprecedented support throughout the journey. It was indeed a joy working with VCU.

Look forward to continue our collaboration further and to strengthen our relationship

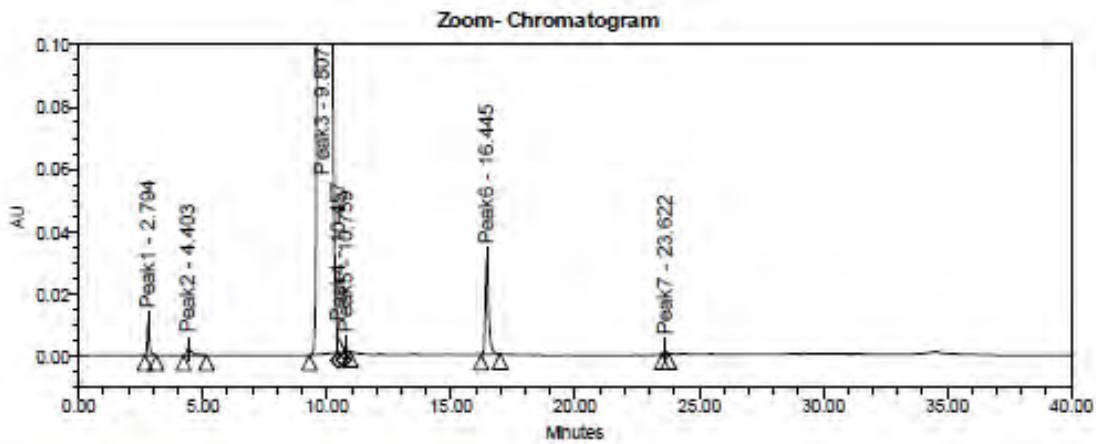
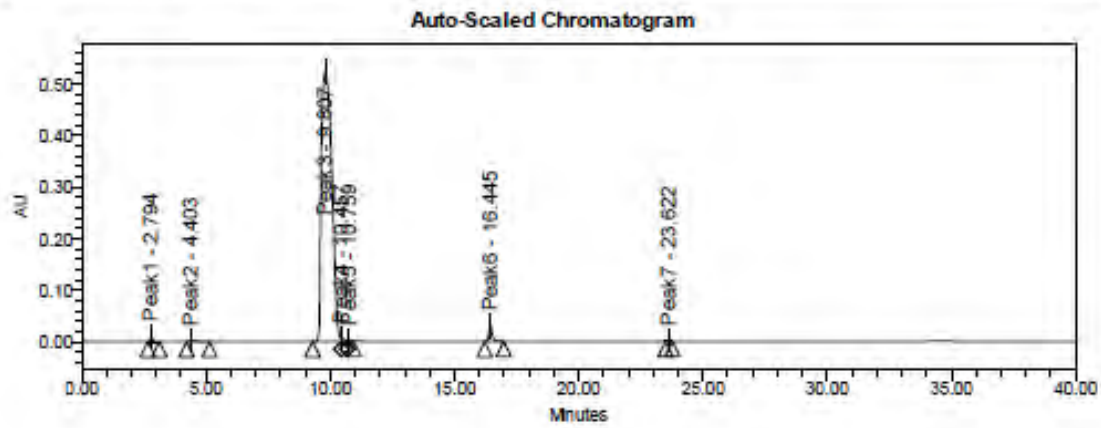
With VCU

Supplementary Documents

Attachment-1_IPC

TCGLS_Report_ZOOM

SAMPLE INFORMATION			
Sample Name:	CRSD-1822-86-Rev2	Acquired By:	SP0113317
Sample Type:	Unknown	Sample Set Name:	TCGLS_180621
Vial:	50	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	280.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 280.0 nm (2998)
Date Acquired:	18-06-2021 10:02:28 IST	Column Name:	XTERRA RP18(250X4.6)mm,5µ
Date Processed:	18-06-2021 11:11:08 IST		



Reported by User: Soumen Pramanik (SP0113317)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 72940
 Page: 1 of 2

Project Name: QCHFL0041
 Date Printed: 18-06-2021
 11:11:40 Asia/Kolkata

Peak Results

	Name	RT	Area	% Area	RT Ratio
1	Peak1	2.794	63375	0.40	0.28
2	Peak2	4.403	34438	0.22	0.45
3	Peak3	9.807	15230065	97.16	1.00
4	Peak4	10.457	41767	0.27	1.07
5	Peak5	10.759	12648	0.08	1.10
6	Peak6	16.445	283909	1.81	1.68
7	Peak7	23.622	8923	0.06	2.41

Reported by User: Soumen Pramanik (SP0113317)
Report Method: TCGLS_Report_ZOOM
Report Method ID: 72940
Page: 2 of 2

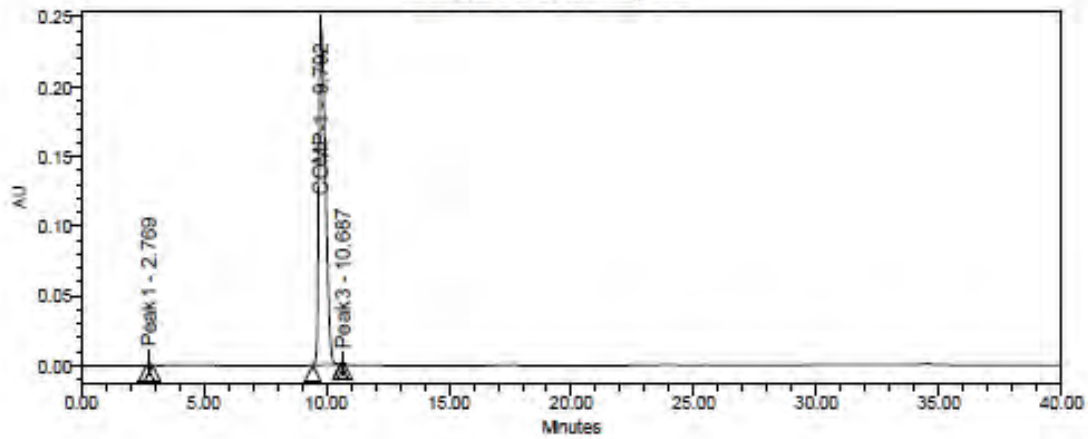
Project Name: QCHPL041
Date Printed:
18-06-2021
11:11:40 Asia/Kolkata

Attachment-2_Pure HPLC

SAMPLE INFORMATION

Sample Name:	CR 99-1522-05-F	Acquired By:	SF0113317
Sample Type:	Unknown	Sample Set Name:	TCGLS_180621
Vial:	7	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2698 PDA 260.0 nm (2968)
Date Acquired:	18-06-2021 18:14:11 IST	Column Name:	XTERRA RP18(250X4.6)mm,5µ
Date Processed:	18-06-2021 20:15:00 IST		

Auto-Scaled Chromatogram



Peak Results

Name	RT	Area	% Area	RT Ratio
1 Peak1	2.769	12737	0.26	0.283
2 COMP-1	9.792	4581545	99.70	1.000
3 Peak3	10.687	1267	0.03	1.091

Reported by User: Amrit Bhadra (AB0113487)
 Report Method: TCGLS_Report
 Report Method ID: 74765
 Page: 1 of 1

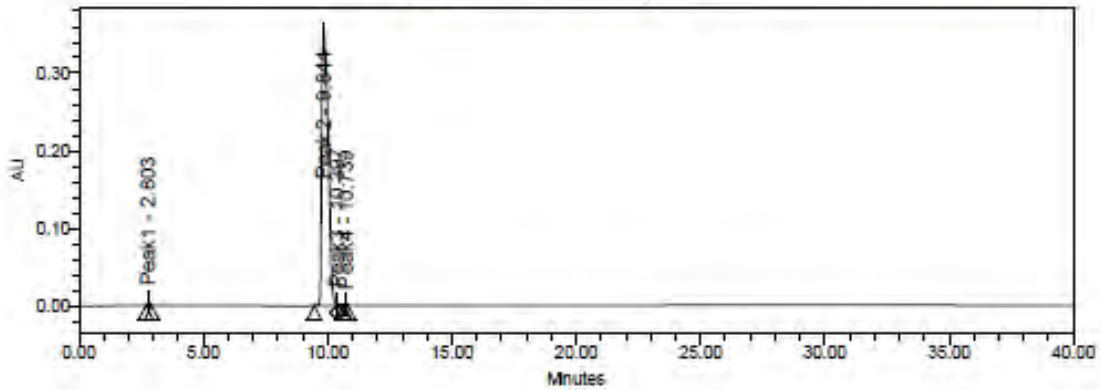
Project Name: QCHPLC041
 Date Printed:
 18-06-2021
 20:15:33 Asia/Kolkata

Attachment-3_Pure HPLC

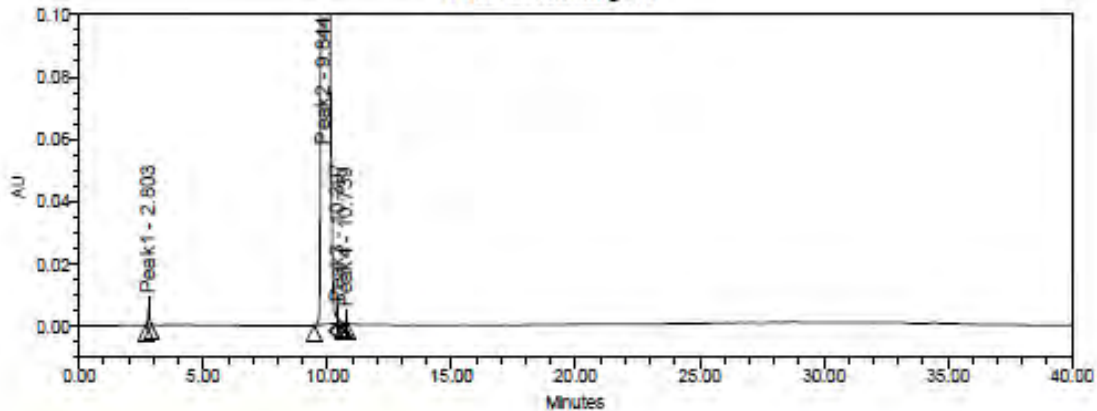
TCGLS_Report_ZOOM

SAMPLE INFORMATION			
Sample Name:	DI980-154813-3-wal	Acquired By:	PG0112811
Sample Type:	Unknown	Sample Set Name:	TCGLS_290621
Vial:	30	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD_
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 260.0 nm (2998)
Date Acquired:	29-06-2021 14:27:21 IST	Column Name:	XTERRA RP18(250x4.6)mm,5µ
Date Processed:	29-06-2021 16:14:06 IST		

Auto-Scaled Chromatogram



Zoom- Chromatogram



Reported by User: Asif Mondal (AM0113345)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 72940
 Page: 1 of 2

Project Name: QCHPLC041
 Date Printed: 29-06-2021
 16:14:38 Asia/Kolkata

Peak Results

	Name	RT	Area	% Area	RT Ratio
1	Peak1	2.803	25679	0.40	0.28
2	Peak2	9.644	6321818	99.41	1.00
3	Peak3	10.397	9985	0.16	1.06
4	Peak4	10.739	1637	0.03	1.09

Reported by User: Asif Mondal (AMD113345)
Report Method: TCGLS_Report_ZOOM
Report Method ID: 72940
Page: 2 of 2

Project Name: QCHPLC041
Date Printed:
29-06-2021
16:14:38 Asia/Kolkata

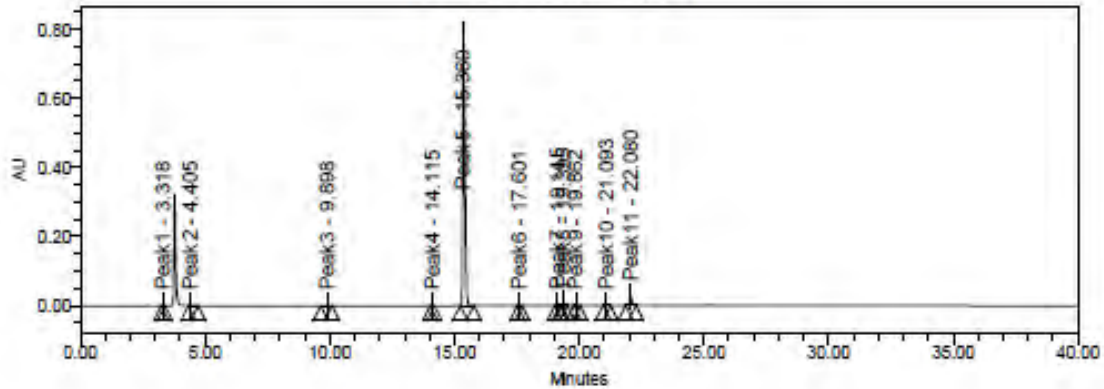
Attachment-4_IPC HPLC

TCGLS_Report_ZOOM

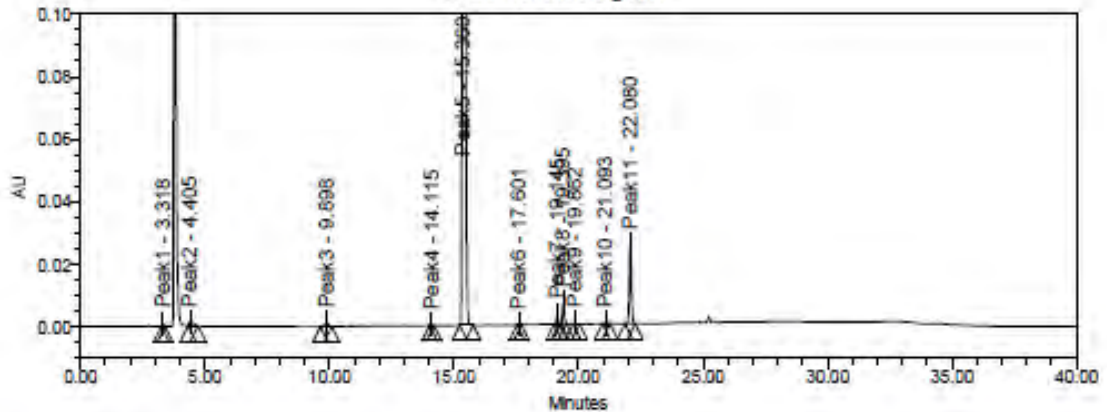
SAMPLE INFORMATION

Sample Name:	01950-19462-6-11M-3	Acquired By:	AM0113345
Sample Type:	Unknown	Sample Set Name:	TCGLS_020721
Vial:	21	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 260.0 nm (2998)
Date Acquired:	03-07-2021 11:04:16 IST	Column Name:	XTERRA RP18(250x4.6)mm,5µ
Date Processed:	03-07-2021 13:35:02 IST		

Auto-Scaled Chromatogram



Zoom- Chromatogram



Reported by User: Asif Mondal (AM0113345)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 72940
 Page: 1 of 2

Project Name: QCHPLC041
 Date Printed: 03-07-2021
 13:54:00 Asia/Kolkata

Peak Results

	Name	RT	Area	% Area	RT Ratio
1	Peak1	3.318	3292	0.06	0.22
2	Peak2	4.405	16431	0.32	0.29
3	Peak3	9.898	12643	0.25	0.64
4	Peak4	14.115	1120	0.02	0.92
5	Peak5	15.360	4859436	95.43	1.00
6	Peak6	17.601	1370	0.03	1.15
7	Peak7	19.145	12048	0.24	1.25
8	Peak8	19.395	34042	0.67	1.26
9	Peak9	19.862	2850	0.06	1.29
10	Peak10	21.093	1725	0.03	1.37
11	Peak11	22.080	146958	2.89	1.44

Reported by User: Asif Mondal (AM0113345)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 72940
 Page: 2 of 2

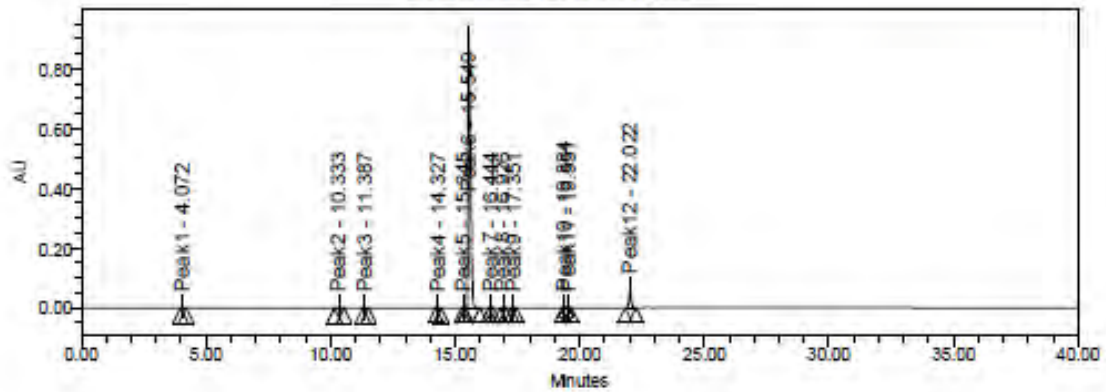
Project Name: QCHPLC041
 Date Printed:
 03-07-2021
 13:54:00 Asia/Kolkata

Attachment-5_ HPLC

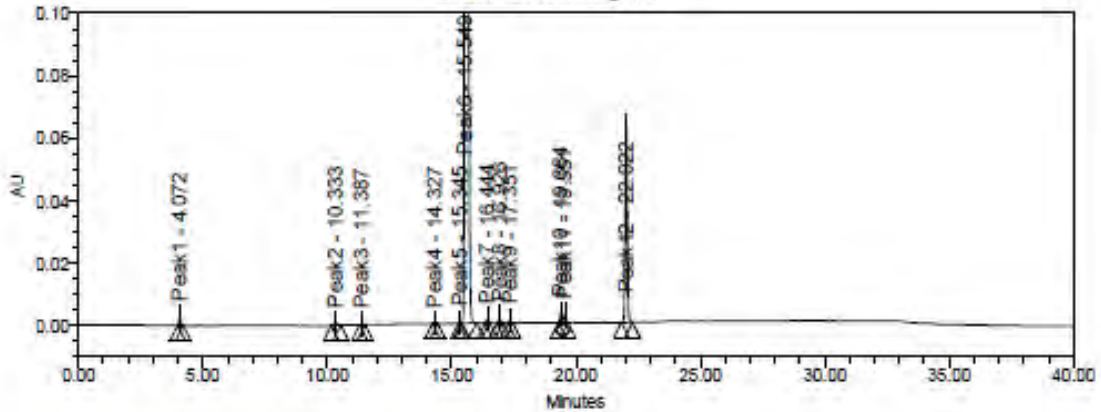
TCGLS_Report_ZOOM

SAMPLE INFORMATION			
Sample Name:	D1902-16421-0-0	Acquired By:	ah0113531
Sample Type:	Unknown	Sample Set Name:	TCGLS_050721
Vial:	3	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 280nm@4.8nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 280nm@4.8nm
Date Acquired:	05-07-2021 10:01:54 IST	Column Name:	XTERRA RP18(250x4.6)mm,5µ
Date Processed:	05-07-2021 10:53:09 IST		

Auto-Scaled Chromatogram



Zoom- Chromatogram



Reported by User: Anirban Hazra (ah0113531)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 72940
 Page: 1 of 2

Project Name: QCHPLC041
 Date Printed: 05-07-2021
 10:54:06 Asia/Kolkata

Peak Results

	Name	RT	Area	% Area	RT Ratio
1	Peak1	4.072	14010	0.20	0.26
2	Peak2	10.333	6653	0.09	0.66
3	Peak3	11.387	1975	0.03	0.73
4	Peak4	14.327	1697	0.02	0.92
5	Peak5	15.345	1543	0.02	0.99
6	Peak6	15.549	6614999	93.83	1.00
7	Peak7	16.444	5876	0.08	1.06
8	Peak8	16.926	8901	0.13	1.09
9	Peak9	17.351	4789	0.07	1.12
10	Peak10	19.384	12153	0.17	1.25
11	Peak11	19.551	14422	0.20	1.26
12	Peak12	22.022	362728	5.15	1.42

Reported by User: Anirban Hazra (ah0113531)
Report Method: TCGLS_Report_ZOOM
Report Method ID: 72940
Page: 2 of 2

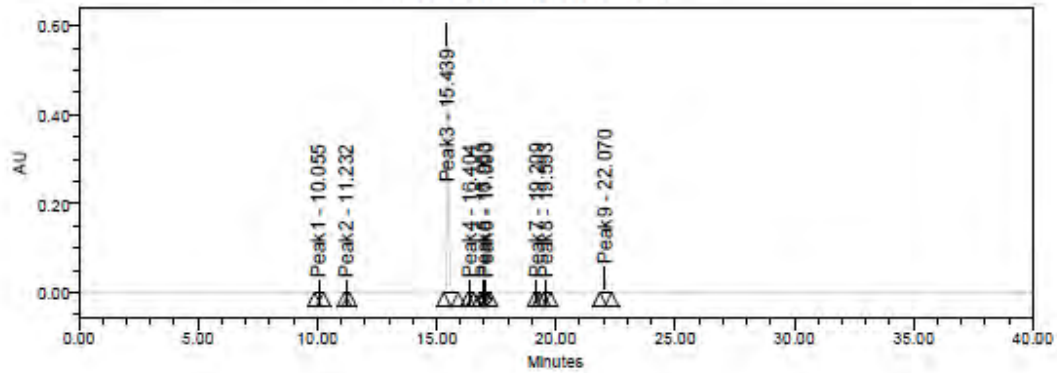
Project Name: QCHPL0041
Date Printed:
05-07-2021
10:54:08 Asia/Kolkata

Attachment-6_ HPLC

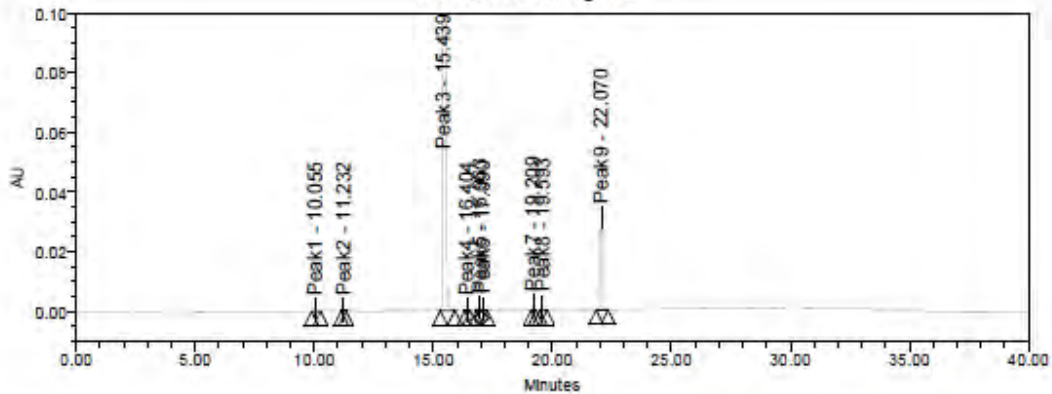
TCGLS_Report_ZOOM

SAMPLE INFORMATION			
Sample Name:	CR90-1940-4-P1	Acquired By:	SP0113317
Sample Type:	Unknown	Sample Set Name:	TCGLS_300821
Vial:	71	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 260.0 nm (2998)
Date Acquired:	01-07-2021 01:12:19 IST	Column Name:	XTERRA RP18(250X4.6)mm,5µ
Date Processed:	01-07-2021 08:02:42 IST		

Auto-Scaled Chromatogram



Zoom- Chromatogram



Reported by User: Sandip Shyam (SS0113486)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 72940
 Page: 1 of 2

Project Name: QCHPLC041
 Date Printed: 01-07-2021
 08:03:23 Asia/Kolkata

Peak Results

	Name	RT	Area	% Area	RT Ratio
1	Peak1	10.055	2980	0.08	0.65
2	Peak2	11.232	943	0.03	0.73
3	Peak3	15.439	3520129	94.59	1.00
4	Peak4	16.404	1190	0.03	1.06
5	Peak5	16.963	4889	0.13	1.10
6	Peak6	17.090	3788	0.10	1.11
7	Peak7	19.209	6086	0.16	1.24
8	Peak8	19.593	7109	0.19	1.27
9	Peak9	22.070	174481	4.69	1.43

Reported by User: Sandip Shyam (SS0113486)
Report Method: TCGLS_Report_ZOOM
Report Method ID: 72940
Page: 2 of 2

Project Name: QCHPLC041
Date Printed:
01-07-2021
08:03:23 Asia/Kolkata

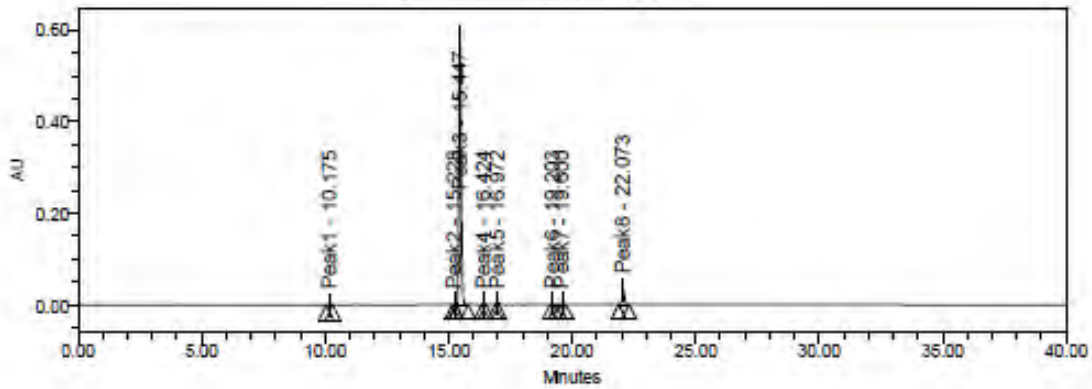
Attachment-7_ HPLC

TCGLS_Report_ZOOM

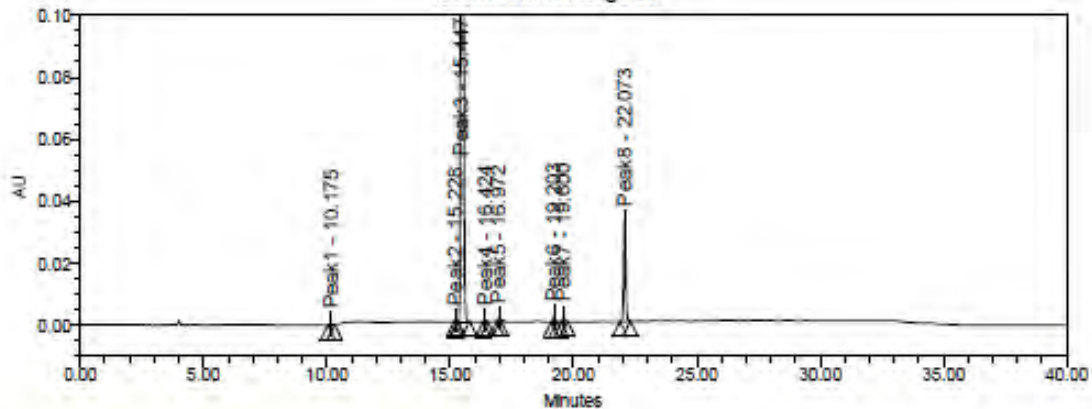
SAMPLE INFORMATION

Sample Name:	CR95-1542-7-P	Acquired By:	SS0113488
Sample Type:	Unknown	Sample Set Name:	TCGLS_010721
Vial:	13	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 260.0 nm (2998)
Date Acquired:	01-07-2021 20:13:15 IST	Column Name:	XTERRA RP18(250X4.6)mm,5µ
Date Processed:	01-07-2021 21:38:14 IST		

Auto-Scaled Chromatogram



Zoom- Chromatogram



Reported by User: Asif Mondal (AMD113345)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 72940
 Page: 1 of 2

Project Name: QCHPLC041
 Date Printed: 01-07-2021
 21:39:11 Asia/Kolkata

Peak Results

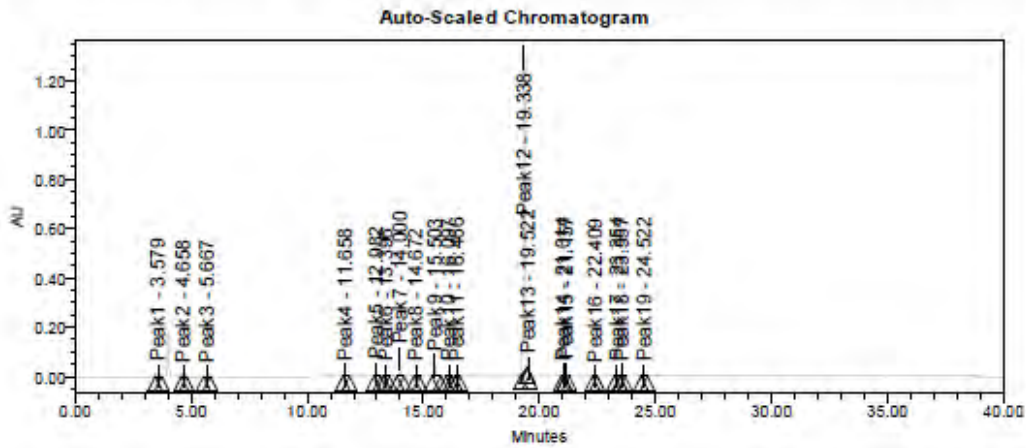
	Name	RT	Area	% Area	RT Ratio
1	Peak1	10.175	2870	0.08	0.66
2	Peak2	15.228	935	0.03	0.99
3	Peak3	15.447	3501094	94.37	1.00
4	Peak4	16.424	2855	0.08	1.06
5	Peak5	16.972	3015	0.08	1.10
6	Peak6	19.203	6642	0.18	1.24
7	Peak7	19.600	8194	0.22	1.27
8	Peak8	22.073	184446	4.97	1.43

Reported by User: Asif Mondal (AM0113345)
Report Method: TCGLS_Report_ZOOM
Report Method ID: 72940
Page: 2 of 2

Project Name: QCHPLC041
Date Printed:
01-07-2021
21:39:11 Asia/Kolkata

Attachment-8_IPC HPLC

SAMPLE INFORMATION			
Sample Name:	CR50-1940-25-Rm-2	Acquired By:	PB0112721
Sample Type:	Unknown	Sample Set Name:	TCGLS_150721A
Vial:	8	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 260.0 nm (2998)
Date Acquired:	15-07-2021 12:41:59 IST	Column Name:	XTERRA RP18(250X4.6)mm,5µ
Date Processed:	15-07-2021 13:48:10 IST		



Peak Results				
Name	RT	Area	% Area	RT Ratio
1 Peak1	3.579	14451	0.19	0.185
2 Peak2	4.658	2575	0.03	0.241
3 Peak3	5.667	3318	0.04	0.293
4 Peak4	11.658	16439	0.22	0.603
5 Peak5	12.982	46026	0.60	0.671
6 Peak6	13.396	5820	0.08	0.693
7 Peak7	14.000	344968	4.51	0.724
8 Peak8	14.672	7381	0.10	0.759
9 Peak9	15.503	205533	2.69	0.802
10 Peak10	16.097	2214	0.03	0.832
11 Peak11	16.466	5702	0.07	0.851

Reported by User: Partha Pratim Bal (PB0112721)
 Report Method: TCGLS_Report
 Report Method ID: 83522
 Page: 1 of 2

Project Name: QCHPLC041
 Date Printed: 15-07-2021
 13:47:03 Asia/Kolkata

Peak Results

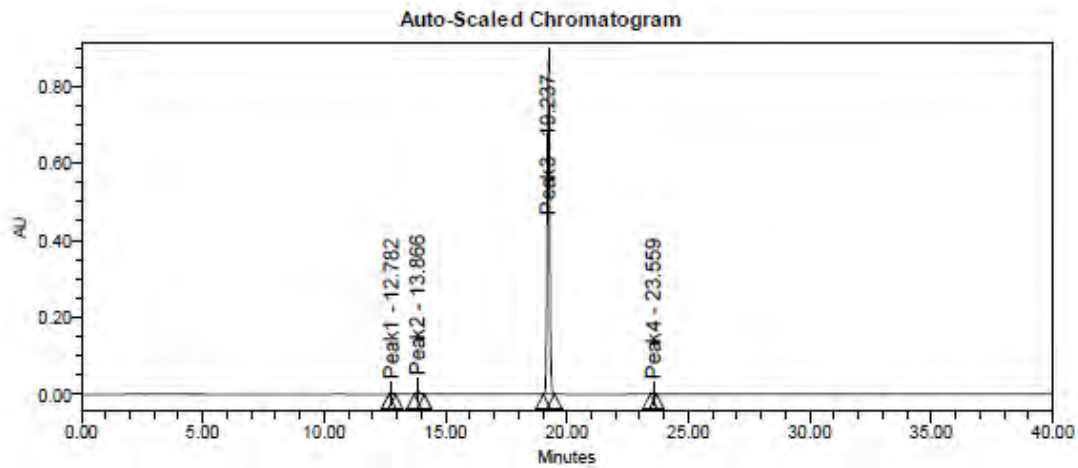
	Name	RT	Area	% Area	RT Ratio
12	Peak12	19.338	6891739	90.15	1.000
13	Peak13	19.522	26979	0.35	1.010
14	Peak14	21.014	7726	0.10	1.087
15	Peak15	21.157	34940	0.46	1.094
16	Peak16	22.409	1279	0.02	1.159
17	Peak17	23.354	6599	0.09	1.208
18	Peak18	23.557	15871	0.21	1.218
19	Peak19	24.522	5577	0.07	1.268

Reported by User: Partha Pratim Bal (PB0112721)
Report Method: TCGLS_Report
Report Method ID: 83522
Page: 2 of 2

Project Name: QCHPLC041
Date Printed:
15-07-2021
13:47:03 Asia/Kolkata

Attachment-9_ HPLC

SAMPLE INFORMATION			
Sample Name:	CR592-16492-26-P	Acquired By:	SC0113139
Sample Type:	Unknown	Sample Set Name:	TCGLS_170721A
Vial:	48	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 260nm@4.8nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 260nm@4.8nm
Date Acquired:	17-07-2021 12:54:39 IST	Column Name:	XTERRA RP18(250X4.6)mm,5µ
Date Processed:	17-07-2021 14:50:15 IST		



Peak Results				
Name	RT	Area	% Area	RT Ratio
1 Peak1	12.782	11519	0.19	0.664
2 Peak2	13.866	65228	1.06	0.721
3 Peak3	19.237	6048936	98.70	1.000
4 Peak4	23.559	3112	0.05	1.225

Reported by User: Soumya chatterjee (SC0113139)
 Report Method: TCGLS_Report
 Report Method ID: 92515
 Page: 1 of 1

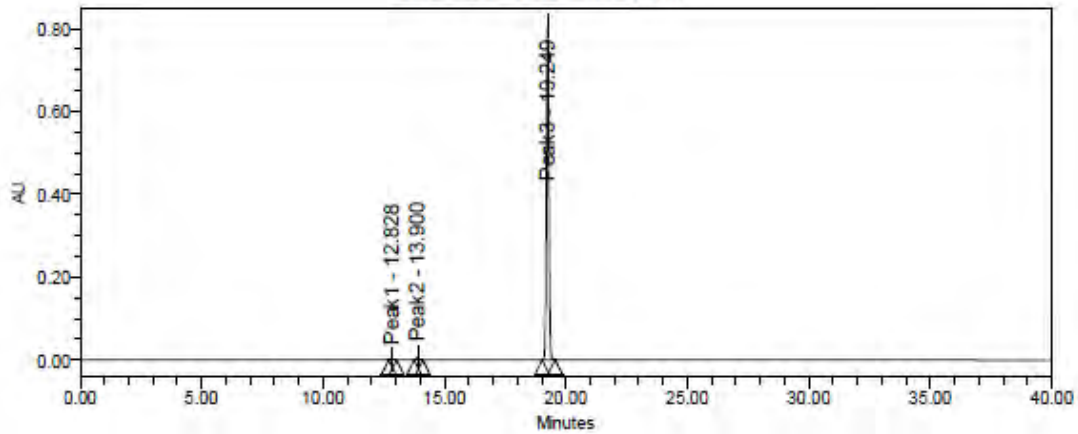
Project Name: QCHPLC041
 Date Printed: 17-07-2021
 14:52:33 Asia/Kolkata

Attachment-10_ HPLC

SAMPLE INFORMATION

Sample Name:	CR552-16492-25-P	Acquired By:	SC0113139
Sample Type:	Unknown	Sample Set Name:	TCGLS_170721A
Vial:	47	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 260nm@4.8nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 260nm@4.8nm
Date Acquired:	17-07-2021 12:13:50 IST	Column Name:	XTERRA RP18(250X4.6)mm,5µ
Date Processed:	17-07-2021 14:48:47 IST		

Auto-Scaled Chromatogram



Peak Results

Name	RT	Area	% Area	RT Ratio
1 Peak1	12.828	7184	0.13	0.666
2 Peak2	13.900	41676	0.74	0.722
3 Peak3	19.249	5565498	99.13	1.000

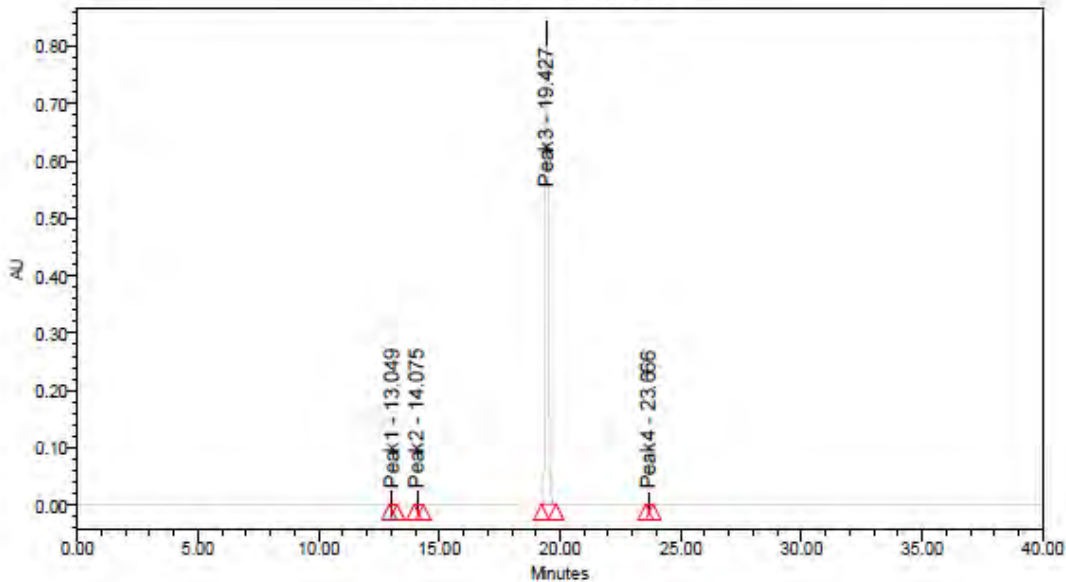
Reported by User: Soumya chatterjee (SC0113139)
 Report Method: TCGLS_Report
 Report Method ID: 92515
 Page: 1 of 1

Project Name: QCHPLC041
 Date Printed: 17-07-2021
 14:51:58 Asia/Kolkata

Attachment-11_ HPLC

SAMPLE INFORMATION			
Sample Name:	CR592-16492-28-P	Acquired By:	SC0113139
Sample Type:	Unknown	Sample Set Name:	TCGLS_200721
Vial:	50	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD_1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 260nm@4.8nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 260nm@4.8nm
Date Acquired:	20-07-2021 10:11:07 IST	Column Name:	XTERRA RP18 (250X4.6)mm, 5u
Date Processed:	20-07-2021 10:55:41 IST		

Auto-Scaled Chromatogram



Peak Results

Name	RT	Area	% Area	RT Ratio
1 Peak1	13.049	27030	0.35	0.672
2 Peak2	14.075	24716	0.32	0.725
3 Peak3	19.427	7585087	99.21	1.000
4 Peak4	23.666	8470	0.11	1.218

Reported by User: Soumya chatterjee (SC0113139)
 Report Method: TCGLS_REPORT
 Report Method ID: 58427
 Page: 1 of 1

Project Name: QCHPLC040
 Date Printed: 20-07-2021
 11:00:44 Asia/Kolkata

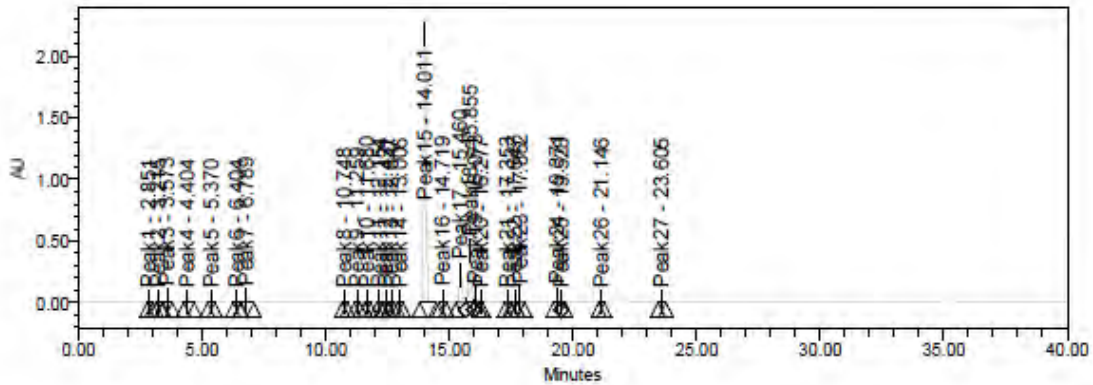
Attachment-12_IPC HPLC

TCGLS_Report_ZOOM

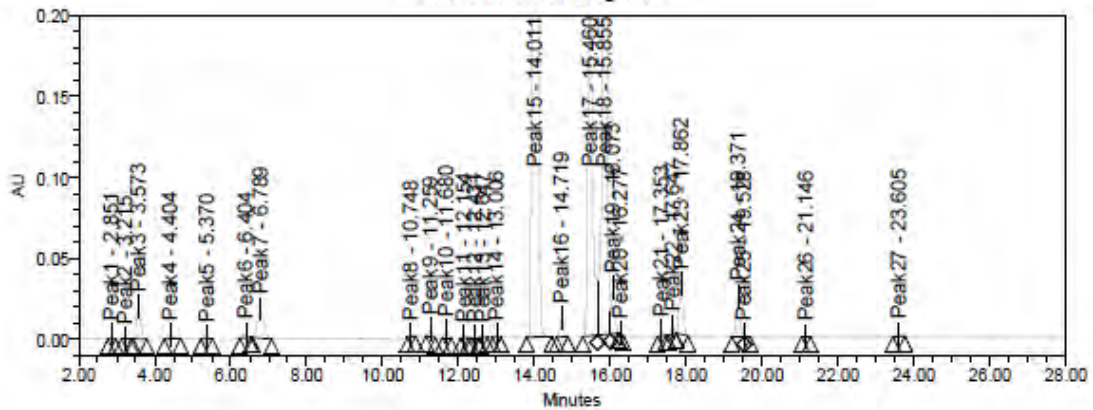
SAMPLE INFORMATION

Sample Name:	CR592-16492-32-Rm2	Acquired By:	SC0113139
Sample Type:	Unknown	Sample Set Name:	TCGLS_220721
Vial:	11	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD_
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 260nm@4.8nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 260nm@4.8nm
Date Acquired:	22-07-2021 15:54:19 IST	Column Name:	XTERRA RP18 (250x4.6)mm, 5u
Date Processed:	22-07-2021 16:54:04 IST		

Auto-Scaled Chromatogram



Zoom- Chromatogram



Reported by User: Partha Sarathi Ghosh (PG0112811)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 58283
 Page: 1 of 2

Project Name: QCHPLC040
 Date Printed: 22-07-2021
 16:55:57 Asia/Kolkata

Peak Results

	Name	RT	Area	% Area	RT Ratio
1	Peak1	2.851	12328	0.06	0.20
2	Peak2	3.215	3313	0.02	0.23
3	Peak3	3.573	148868	0.71	0.25
4	Peak4	4.404	28051	0.12	0.31
5	Peak5	5.370	12026	0.06	0.38
6	Peak6	6.404	20459	0.10	0.46
7	Peak7	6.789	222514	1.06	0.48
8	Peak8	10.748	9063	0.04	0.77
9	Peak9	11.259	28928	0.14	0.80
10	Peak10	11.680	25004	0.12	0.83
11	Peak11	12.154	2582	0.01	0.87
12	Peak12	12.431	1979	0.01	0.89
13	Peak13	12.847	1897	0.01	0.90
14	Peak14	13.008	8078	0.04	0.93
15	Peak15	14.011	14501055	69.31	1.00
16	Peak16	14.719	77680	0.37	1.05
17	Peak17	15.460	1884602	9.01	1.10
18	Peak18	15.855	3258239	15.57	1.13
19	Peak19	16.073	186535	0.89	1.15
20	Peak20	16.277	4783	0.02	1.16
21	Peak21	17.353	20912	0.10	1.24
22	Peak22	17.847	30084	0.14	1.26
23	Peak23	17.862	226801	1.08	1.27
24	Peak24	19.371	192124	0.92	1.38
25	Peak25	19.528	4734	0.02	1.39
26	Peak26	21.146	2356	0.01	1.51
27	Peak27	23.605	10085	0.05	1.68

Reported by User: Partha Sarathi Ghosh (PG0112811)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 58283
 Page: 2 of 2

Project Name: QCHPLC040
 Date Printed:
 22-07-2021
 16:55:57 Asia/Kolkata

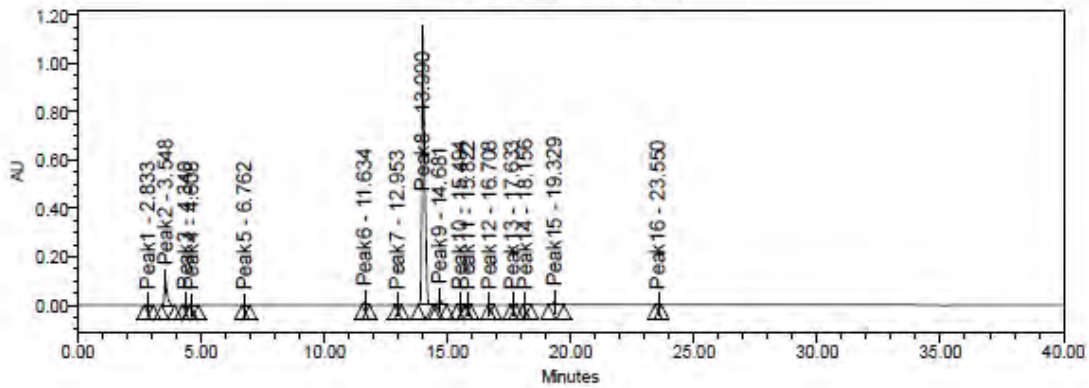
Attachment-13_ HPLC

TCGLS_Report_ZOOM

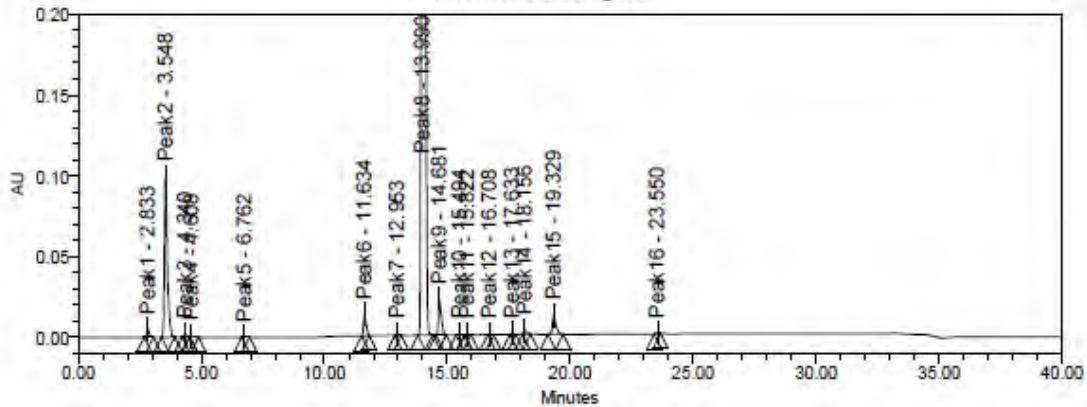
SAMPLE INFORMATION

Sample Name:	CR552-16482-32-CR2	Acquired By:	SP0113317
Sample Type:	Unknown	Sample Set Name:	TCGLS_260721A
Vial:	6	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD_
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 260nm@4.8nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 260nm@4.8nm
Date Acquired:	26-07-2021 15:18:07 IST	Column Name:	XTERRA RP18 (250X4.6)mm, 5u
Date Processed:	26-07-2021 16:09:04 IST		

Auto-Scaled Chromatogram



Zoom- Chromatogram



Reported by User: Asif Mondal (AM0113345)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 59330
 Page: 1 of 2

Project Name: QCHPLC040
 Date Printed: 26-07-2021
 16:09:56 Asia/Kolkata

Peak Results

	Name	RT	Area	% Area	RT Ratio
1	Peak1	2.833	31886	0.31	0.20
2	Peak2	3.548	797826	7.81	0.25
3	Peak3	4.340	12842	0.13	0.31
4	Peak4	4.608	4705	0.05	0.33
5	Peak5	6.762	2169	0.02	0.48
6	Peak6	11.634	98708	0.97	0.83
7	Peak7	12.953	7851	0.08	0.93
8	Peak8	13.990	8927829	87.43	1.00
9	Peak9	14.681	179315	1.76	1.05
10	Peak10	15.494	3178	0.03	1.11
11	Peak11	15.822	2902	0.03	1.13
12	Peak12	16.708	1675	0.02	1.19
13	Peak13	17.633	6245	0.06	1.26
14	Peak14	18.156	17339	0.17	1.30
15	Peak15	19.329	113263	1.11	1.38
16	Peak16	23.550	3417	0.03	1.88

Reported by User: Asif Mondal (AM0113345)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 59330
 Page: 2 of 2

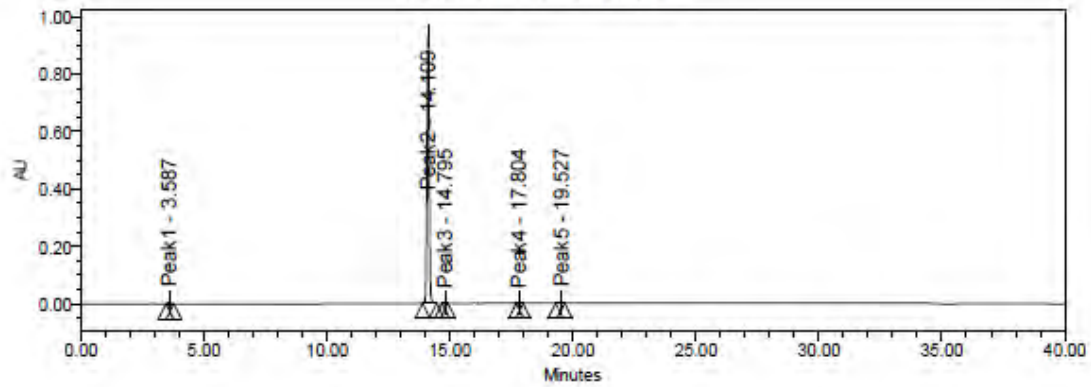
Project Name: QCHPLC040
 Date Printed:
 26-07-2021
 16:09:56 Asia/Kolkata

Attachment-14_ HPLC

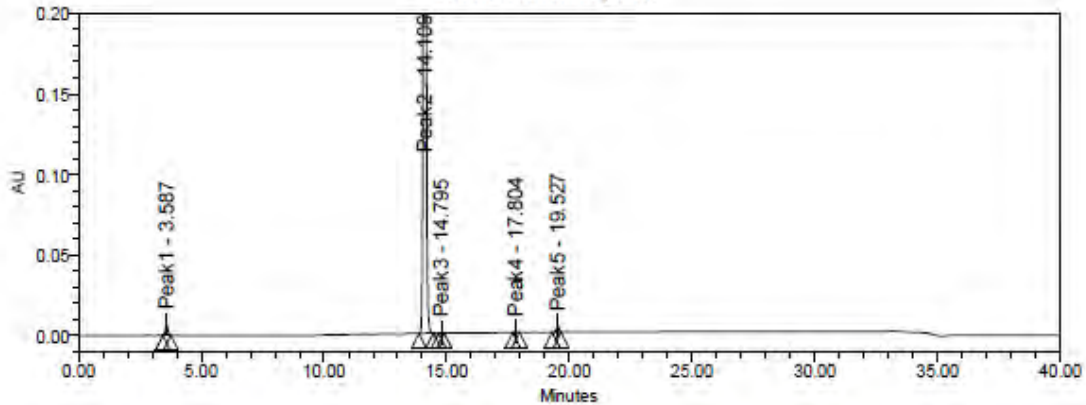
TCGLS Report ZOOM

SAMPLE INFORMATION			
Sample Name:	CR992-15482-32-F1	Acquired By:	AM0113345
Sample Type:	Unknown	Sample Set Name:	TCGLS_280721A
Vial:	28	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD_
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 260nm@4.8nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 260nm@4.8nm
Date Acquired:	28-07-2021 20:18:47 IST	Column Name:	XTERRA RP18 (250X4.6)mm, 5u
Date Processed:	28-07-2021 21:15:03 IST		

Auto-Scaled Chromatogram



Zoom- Chromatogram



Reported by User: Asif Mondal (AM0113345)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 59330
 Page: 1 of 2

Project Name: QCHPLC040
 Date Printed: 28-07-2021
 21:15:39 Asia/Kolkata

Peak Results

	Name	RT	Area	% Area	RT Ratio
1	Peak1	3.587	50560	0.83	0.25
2	Peak2	14.109	6018708	98.62	1.00
3	Peak3	14.795	1847	0.03	1.05
4	Peak4	17.804	4019	0.07	1.26
5	Peak5	19.527	27796	0.46	1.38

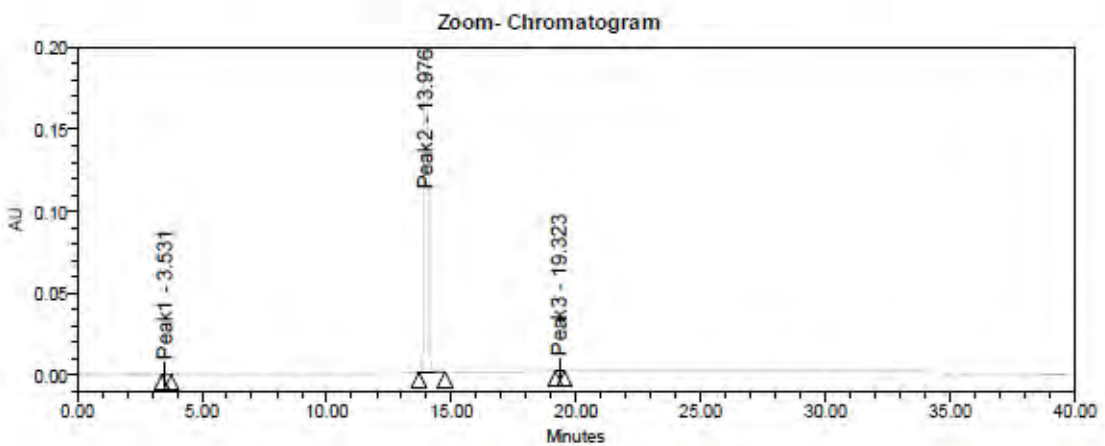
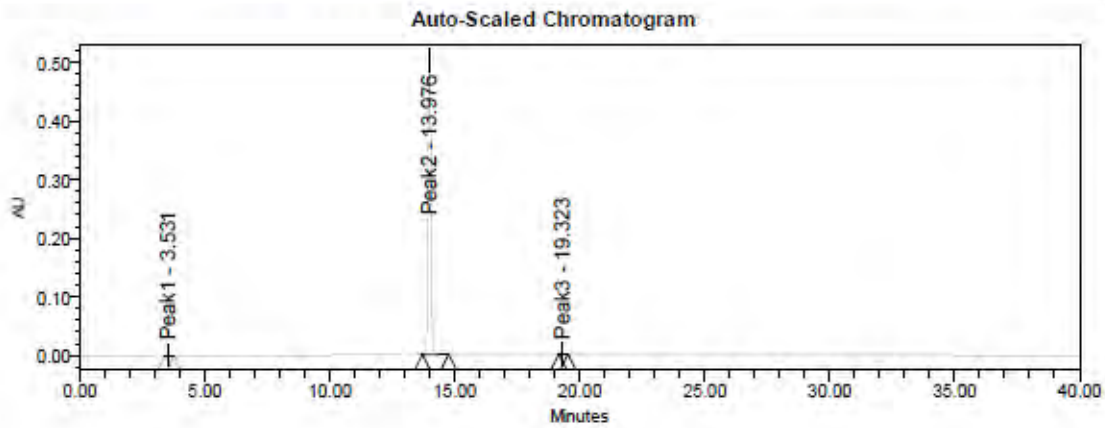
Reported by User: Asif Mondal (AM0113345)
Report Method: TCGLS_Report_ZOOM
Report Method ID: 59330
Page: 2 of 2

Project Name: QCHPLC040
Date Printed:
28-07-2021
21:15:39 Asia/Kolkata

Attachment-15_HPLC

TCGLS_Report_ZOOM

SAMPLE INFORMATION			
Sample Name:	CR52-16482-32-p	Acquired By:	ah0113531
Sample Type:	Unknown	Sample Set Name:	TCGLS_030821
Vial:	46	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD_
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 260nm@4.8nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 260nm@4.8nm
Date Acquired:	03-08-2021 12:39:45 IST	Column Name:	XTERRA RP18 (250x4.6)mm, 5u
Date Processed:	03-08-2021 14:30:47 IST		



Reported by User: Sandip Shyam (SS0113466)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 60854
 Page: 1 of 2

Project Name: QCHPLC040
 Date Printed: 03-08-2021
 14:32:42 Asia/Kolkata

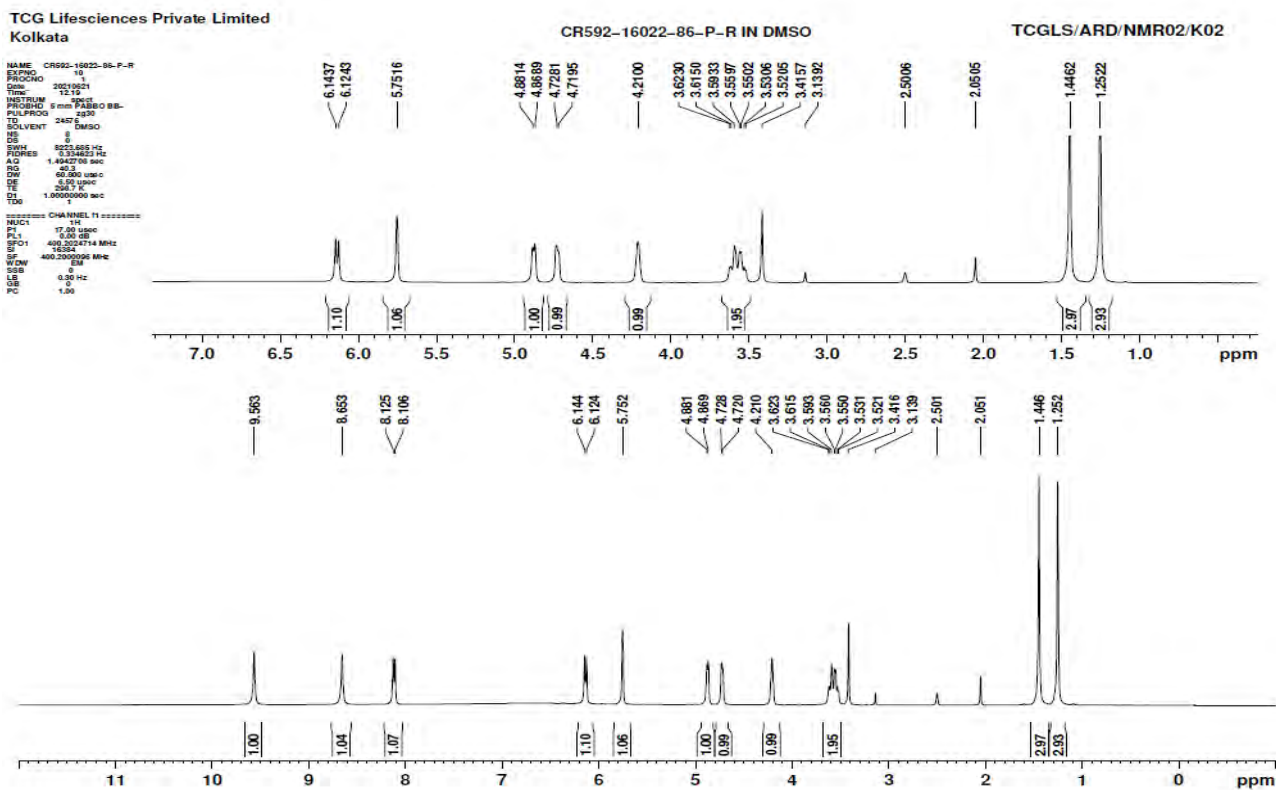
Peak Results

	Name	RT	Area	% Area	RT Ratio
1	Peak1	3.531	3889	0.09	0.25
2	Peak2	13.976	4212535	99.83	1.00
3	Peak3	19.323	3195	0.08	1.38

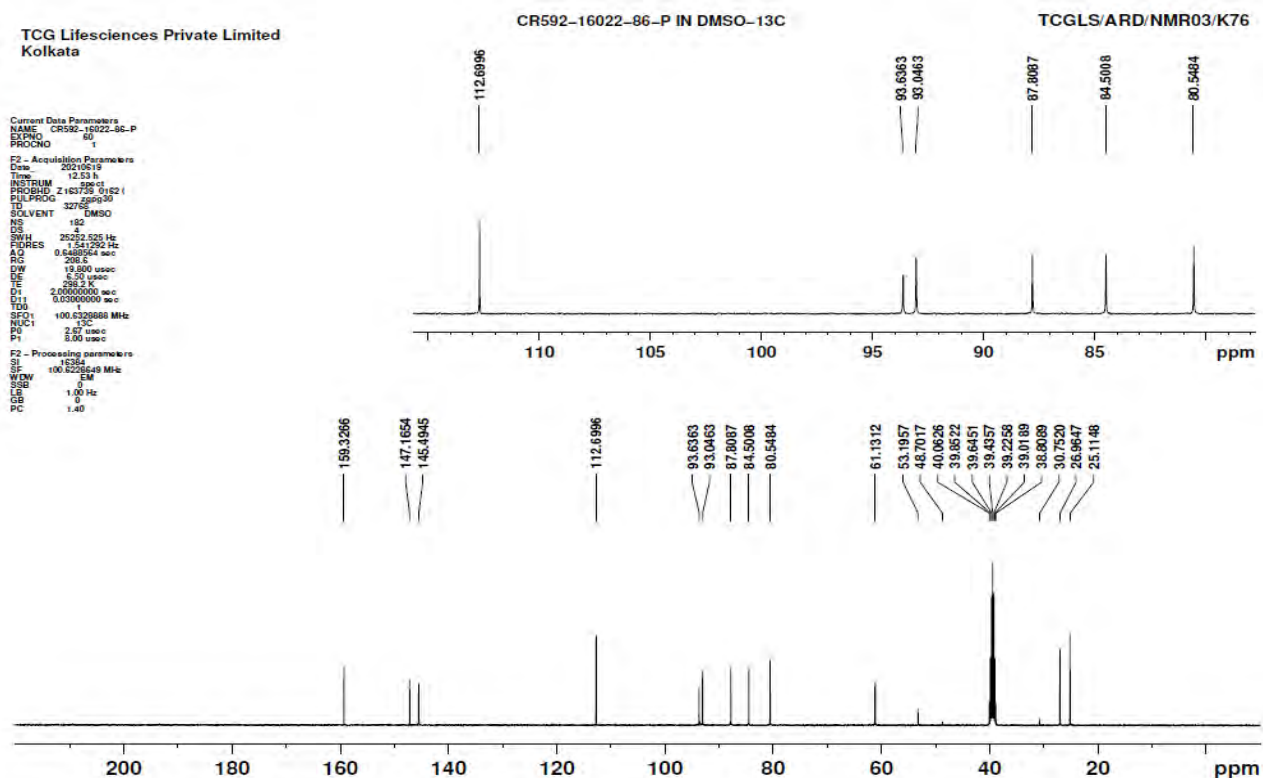
Reported by User: Sandip Shyam (SS0113466)
Report Method: TCGLS_Report_ZOOM
Report Method ID: 60854
Page: 2 of 2

Project Name: QCHPLC040
Date Printed:
03-08-2021
14:32:42 Asia/Kolkata

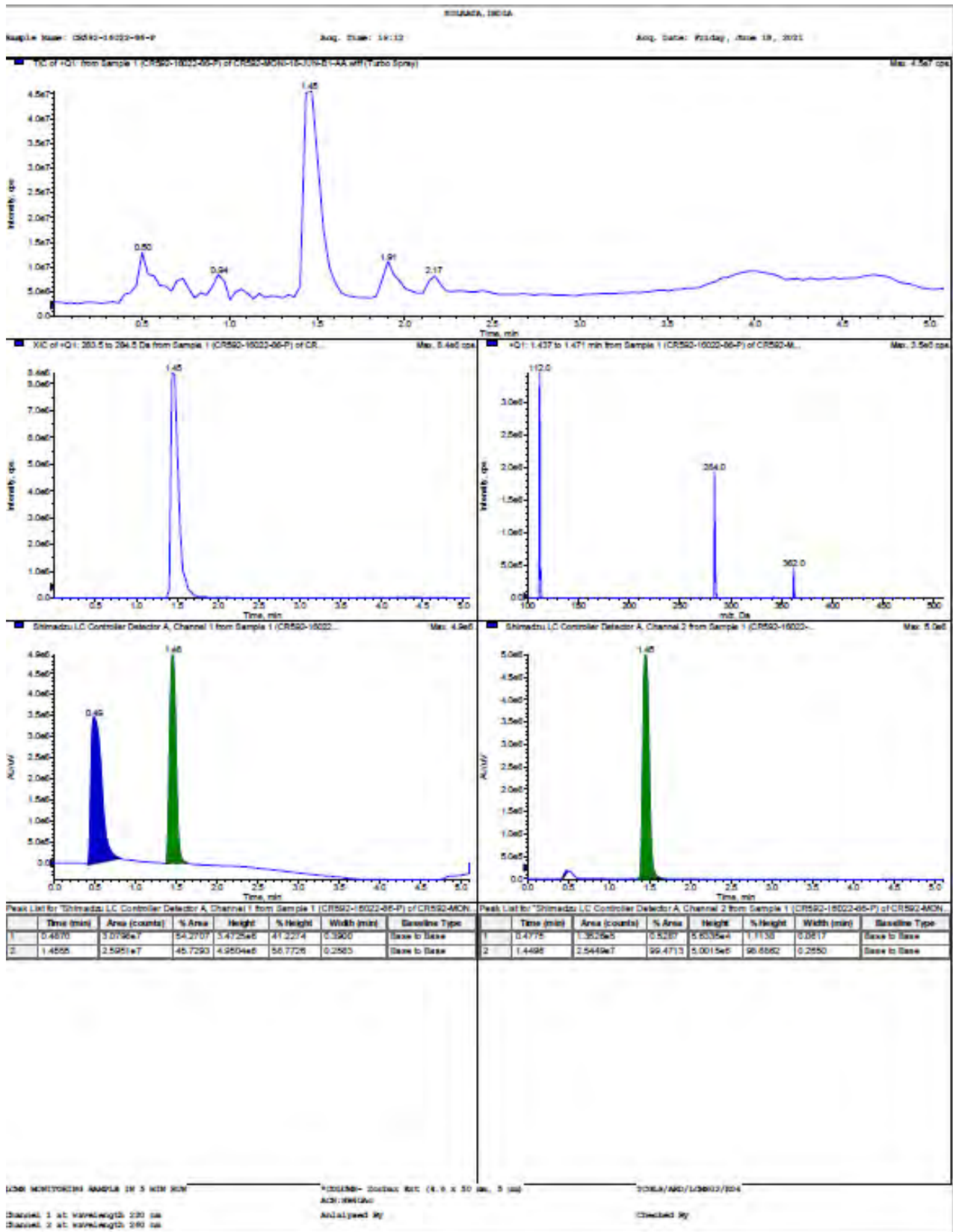
Attachment-16_1HNMR



Attachment-17_13C NMR



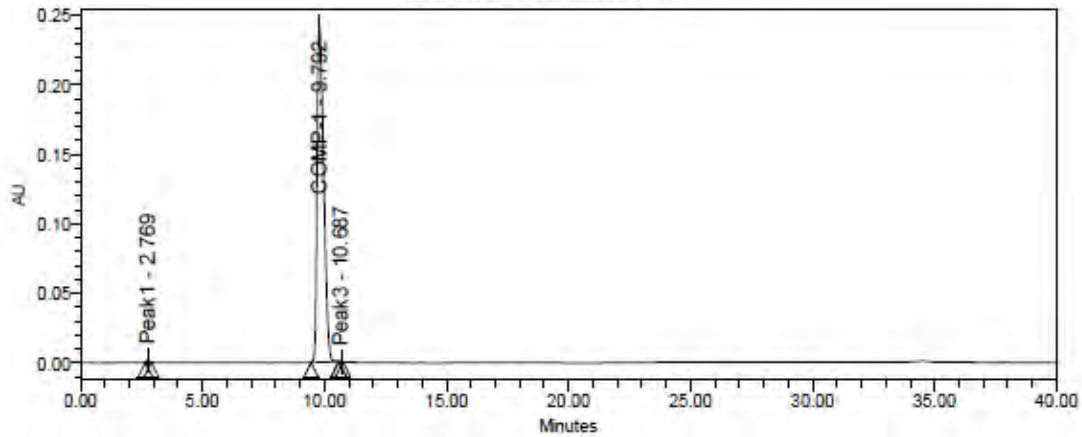
Attachment-18-LCMS



Attachment-19_HPLC

SAMPLE INFORMATION			
Sample Name:	CR992-19022-96-F	Acquired By:	SP0113317
Sample Type:	Unknown	Sample Set Name:	TCGLS_180621
Vial:	7	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 260.0 nm (2998)
Date Acquired:	18-06-2021 18:14:11 IST	Column Name:	XTERRA RP18(250X4.6)mm,5µ
Date Processed:	18-06-2021 20:15:00 IST		

Auto-Scaled Chromatogram



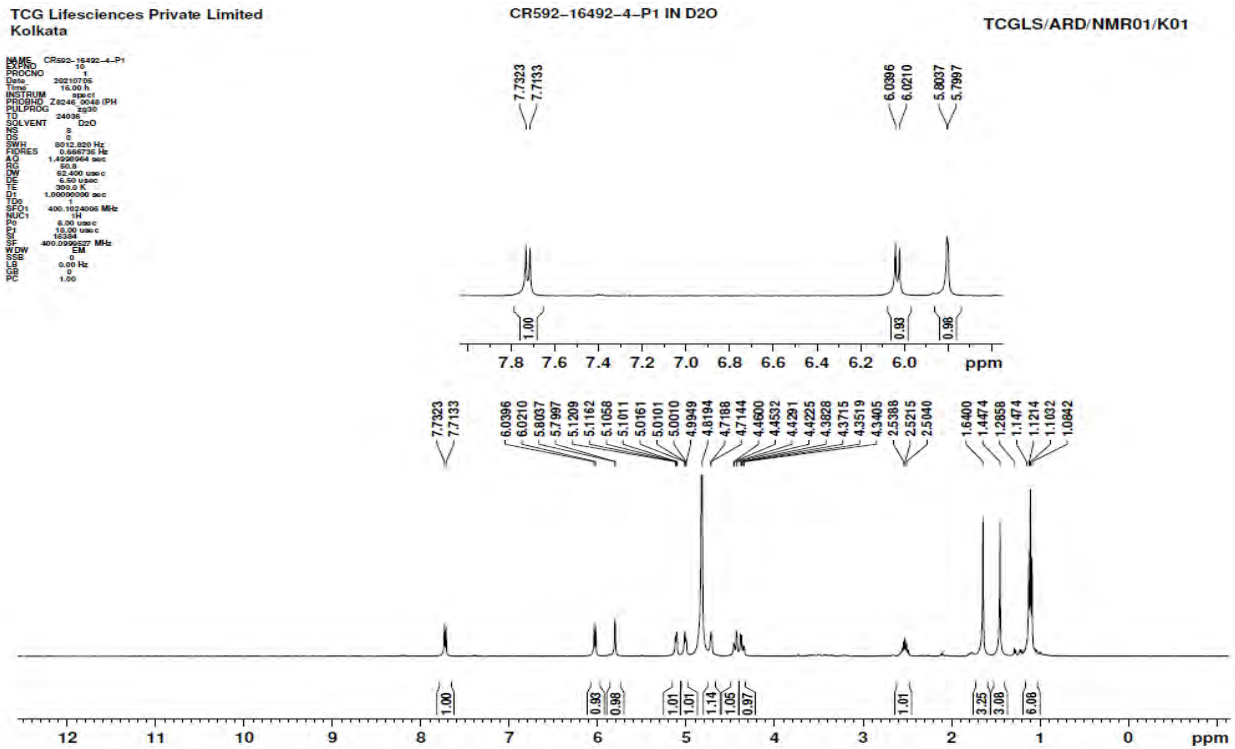
Peak Results

Name	RT	Area	% Area	RT Ratio
1 Peak1	2.769	12737	0.28	0.283
2 COMP-1	9.792	4581545	99.70	1.000
3 Peak3	10.687	1267	0.03	1.091

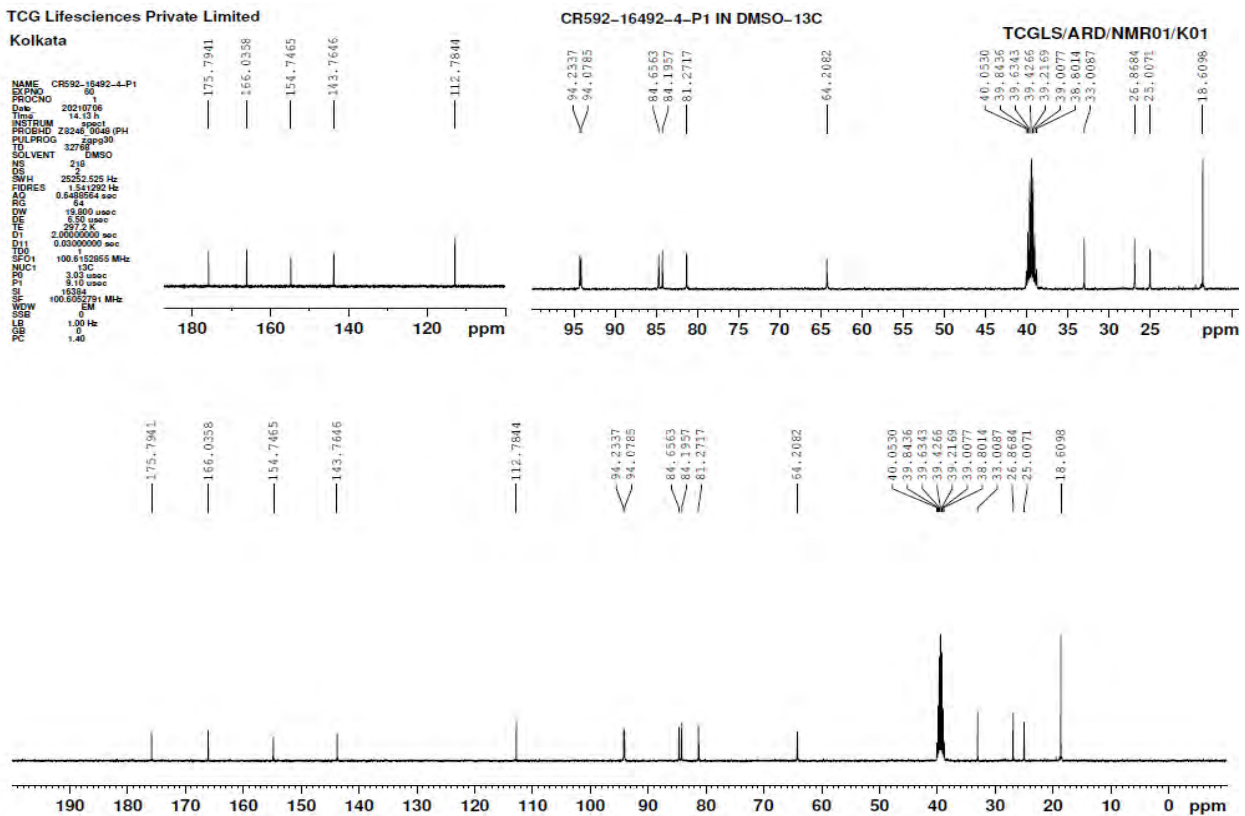
Reported by User: Amrit Bhadra (AB0113467)
 Report Method: TCGLS_Report
 Report Method ID: 74765
 Page: 1 of 1

Project Name: QCHPLC041
 Date Printed: 18-06-2021
 20:15:33 Asia/Kolkata

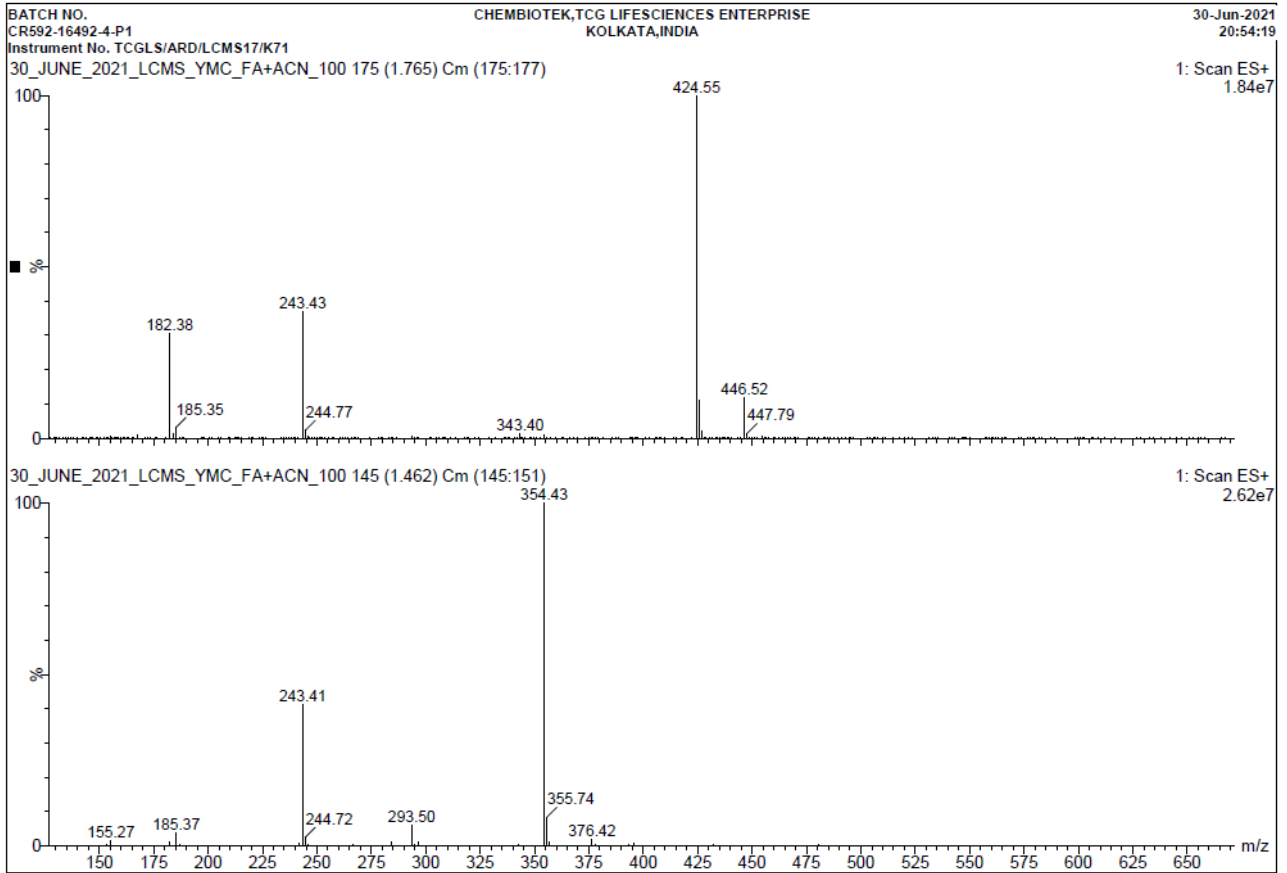
Attachment-20-1HNMR



Attachment-21-13CNMR



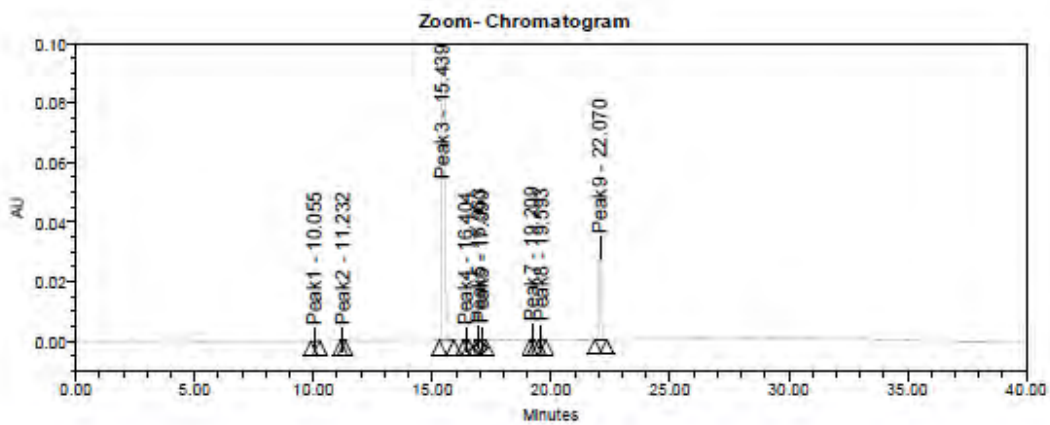
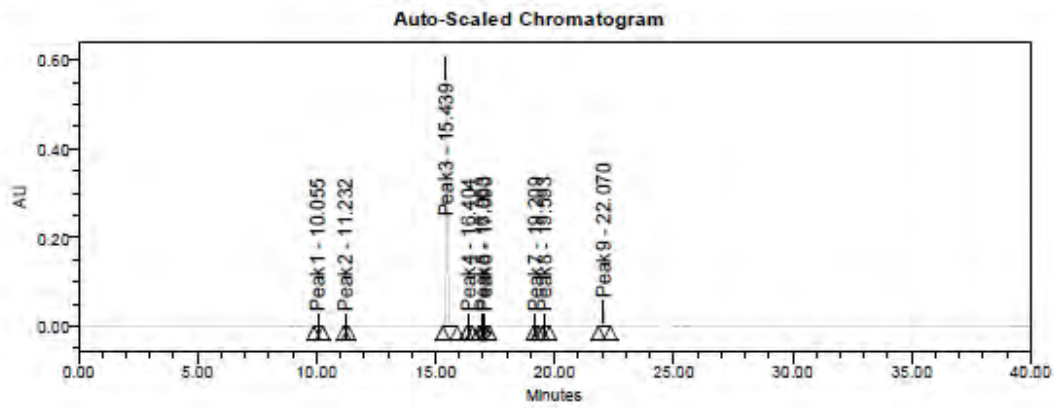
Attachment-22-LCMS



Attachment-23-HPLC

TCGLS_Report_ZOOM

SAMPLE INFORMATION			
Sample Name:	CR50-16402-4-F11	Acquired By:	SP0113317
Sample Type:	Unknown	Sample Set Name:	TCGLS_300621
Vial:	71	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 260.0 nm (2998)
Date Acquired:	01-07-2021 01:12:19 IST	Column Name:	XTERRA RP18(250x4.6)mm,5µ
Date Processed:	01-07-2021 08:02:42 IST		



Reported by User: Sandip Shyam (SS0113466)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 72940
 Page: 1 of 2

Project Name: QCHPLC041
 Date Printed: 01-07-2021
 08:03:23 Asia/Kolkata

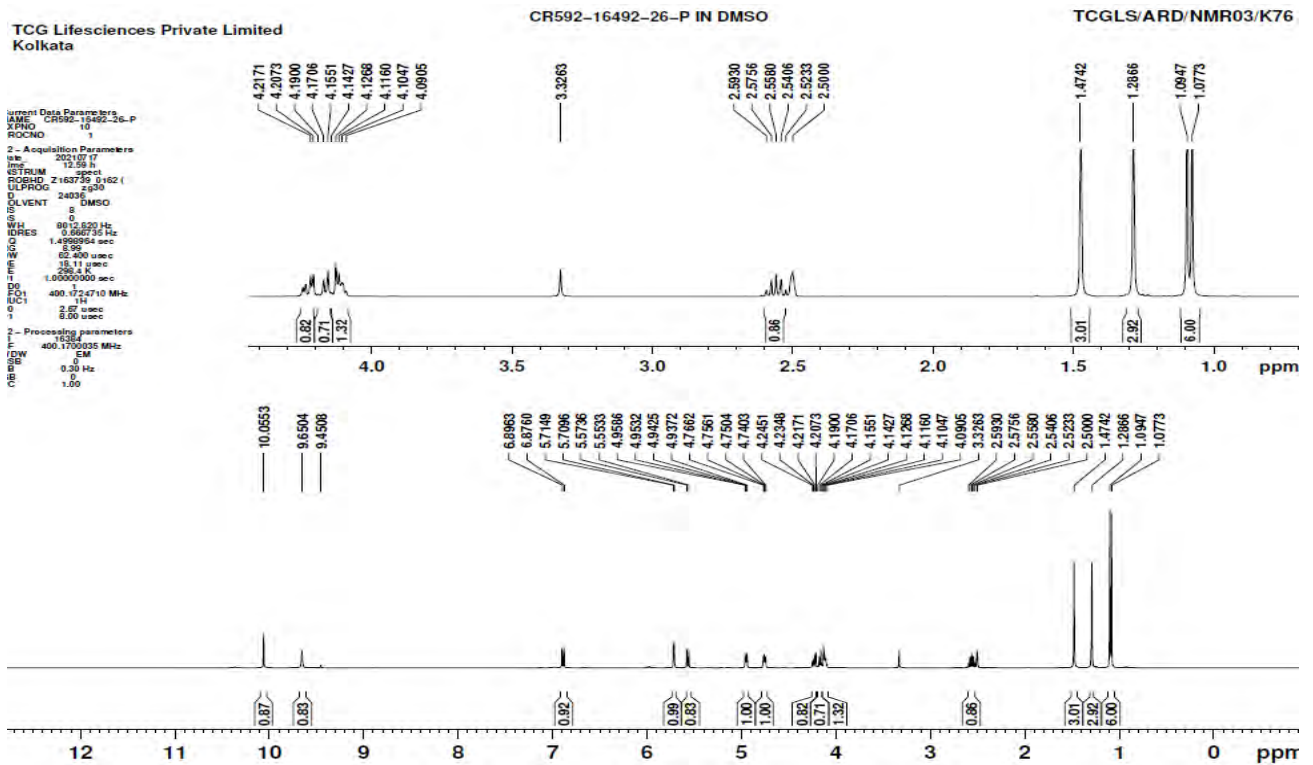
Peak Results

	Name	RT	Area	% Area	RT Ratio
1	Peak1	10.055	2980	0.08	0.65
2	Peak2	11.232	943	0.03	0.73
3	Peak3	15.439	3520129	94.59	1.00
4	Peak4	16.404	1190	0.03	1.06
5	Peak5	16.963	4889	0.13	1.10
6	Peak6	17.090	3788	0.10	1.11
7	Peak7	19.209	6086	0.16	1.24
8	Peak8	19.593	7109	0.19	1.27
9	Peak9	22.070	174481	4.69	1.43

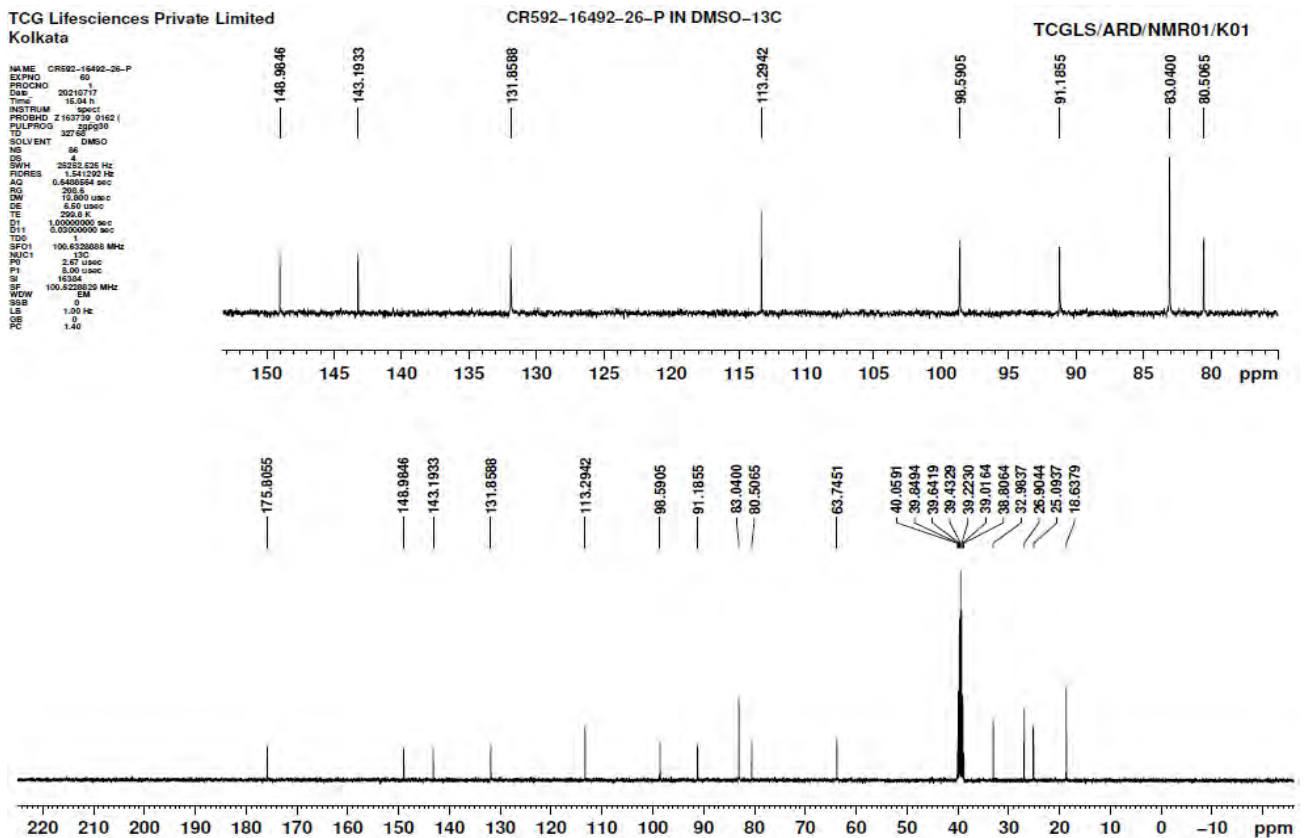
Reported by User: Sandip Shyam (SS0113486)
Report Method: TCGLS_Report_ZOOM
Report Method ID: 72940
Page: 2 of 2

Project Name: QCHPLC041
Date Printed:
01-07-2021
08:03:23 Asia/Kolkata

Attachment-24-1HNMR



Attachment-25-13CNMR



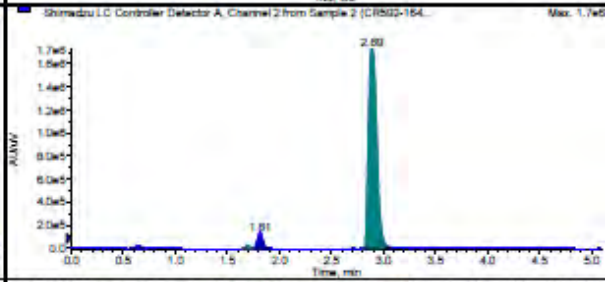
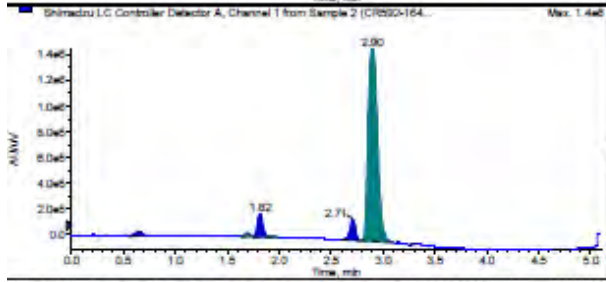
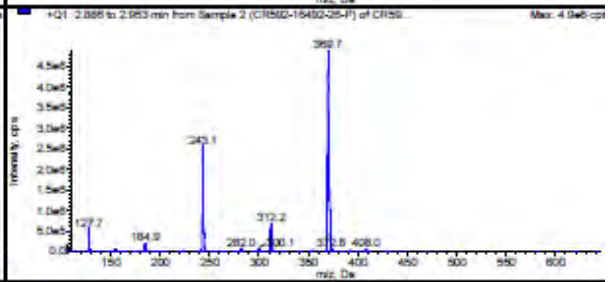
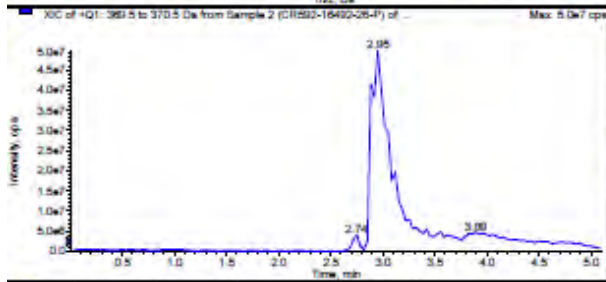
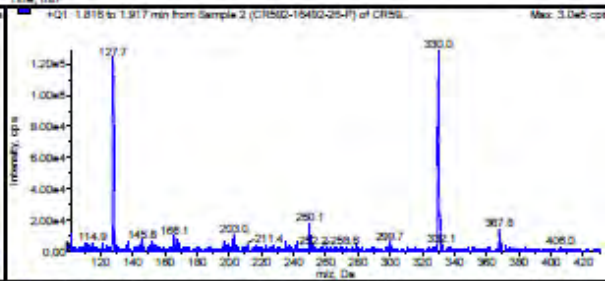
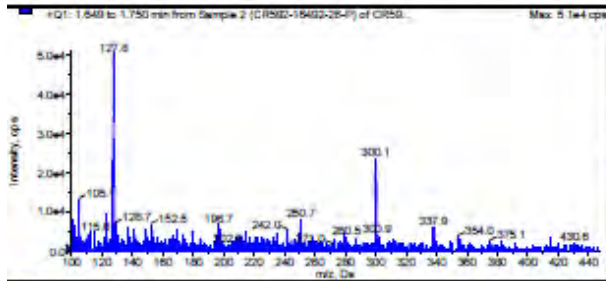
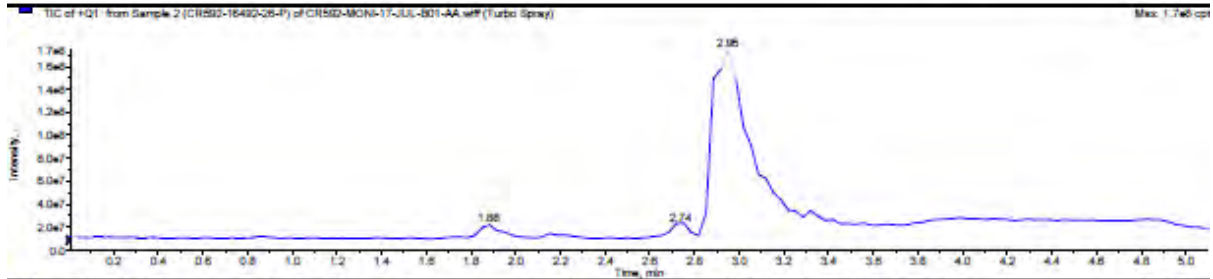
Attachment-26-LCMS

CHEMBIOTEK A TCG Lifesciences Enterprise,KOLKATA,INDIA

Sample Name: CR592-16492-26-P

Acq. Time: 12:55

Acq. Date: Saturday, July 17, 2021



Peak List for "Shimadzu LC Controller Detector A, Channel 1 from Sample 2 (CR592-16492-26-P) of CR592-M"

Time (min)	Area (counts)	%Area	Height	%Height	Width (min)	Baseline Type
0.8490	1.3362e5	1.2917	3.2454e4	1.8965	0.1450	Base to Base
1.8954	1.0453e5	1.5028	3.0339e4	1.5829	0.1217	Valley
1.8185	6.4308e5	6.1681	1.8155e5	9.4983	0.1267	Edge, Skim
1.8283	3.4807e4	0.3338	1.0817e4	0.5707	0.1033	Edge, Daughter
2.7384	5.5310e5	5.3051	1.5929e5	8.3270	0.1750	Valley
2.8984	8.9503e6	85.8482	1.4385e6	78.1828	0.3167	Valley
3.2385	2517.0784	0.0225	2892.8863	0.1407	0.0587	Base to Base

Peak List for "Shimadzu LC Controller Detector A, Channel 2 from Sample 2 (CR592-16492-26-P) of CR592-M"

Time (min)	Area (counts)	%Area	Height	%Height	Width (min)	Baseline Type
0.8493	1.1189e5	1.1313	2.7833e4	1.4433	0.1400	Base to Base
1.8933	7.2339e4	0.7314	2.2972e4	1.1909	0.1083	Valley
1.8138	4.8550e5	4.7097	1.3947e5	7.2844	0.1450	Valley
2.8897	9.2402e6	89.4275	1.7245e6	90.0724	0.2717	Base to Base

LCMS MONITORING SAMPLE IN 5 MIN RUN

*COLUMN- X-Bridge-C8 (4.6X50mm, 5µm)
ACN:PHOAc

TCGLSARD/LCMS15K72

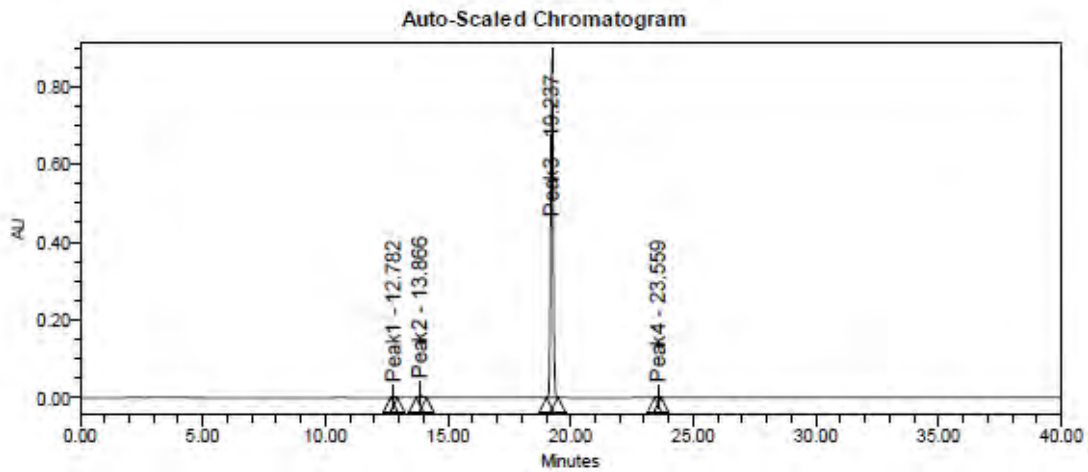
Channel 1 at wavelength 220 nm
Channel 2 at wavelength 260 nm

Analysed By

Checked By

Attachment-27-HPLC

SAMPLE INFORMATION			
Sample Name:	CR552-16432-25-P	Acquired By:	SC0113139
Sample Type:	Unknown	Sample Set Name:	TCGLS_170721A
Vial:	48	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 260nm@4.8nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 260nm@4.8nm
Date Acquired:	17-07-2021 12:54:39 IST	Column Name:	XTERRA RP18(250X4.6)mm,5µ
Date Processed:	17-07-2021 14:50:15 IST		



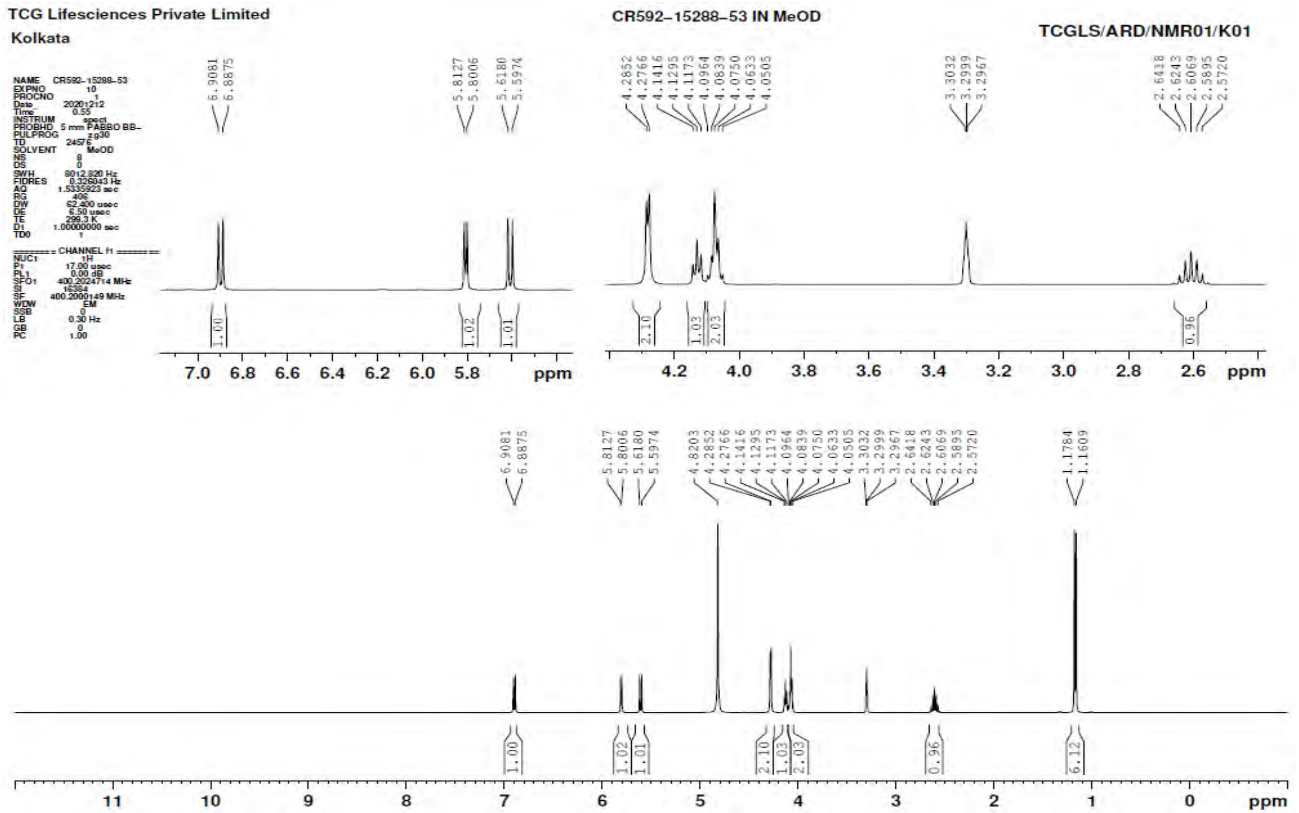
Peak Results

Name	RT	Area	% Area	RT Ratio
1 Peak1	12.782	11519	0.19	0.664
2 Peak2	13.866	65229	1.06	0.721
3 Peak3	19.237	6048936	98.70	1.000
4 Peak4	23.559	3112	0.05	1.225

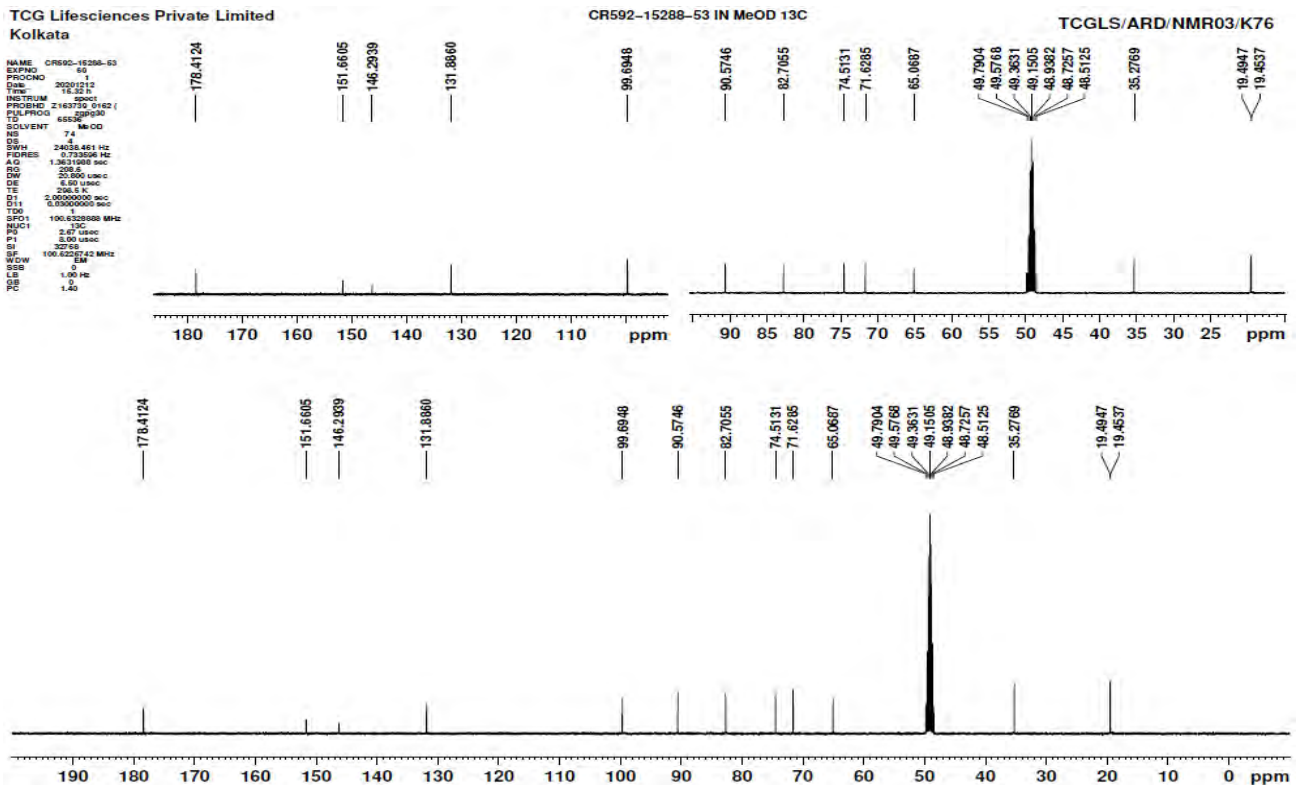
Reported by User: Soumya chatterjee (SC0113139)
 Report Method: TCGLS_Report
 Report Method ID: 92515
 Page: 1 of 1

Project Name: QCHPLC041
 Date Printed: 17-07-2021
 14:52:33 Asia/Kolkata

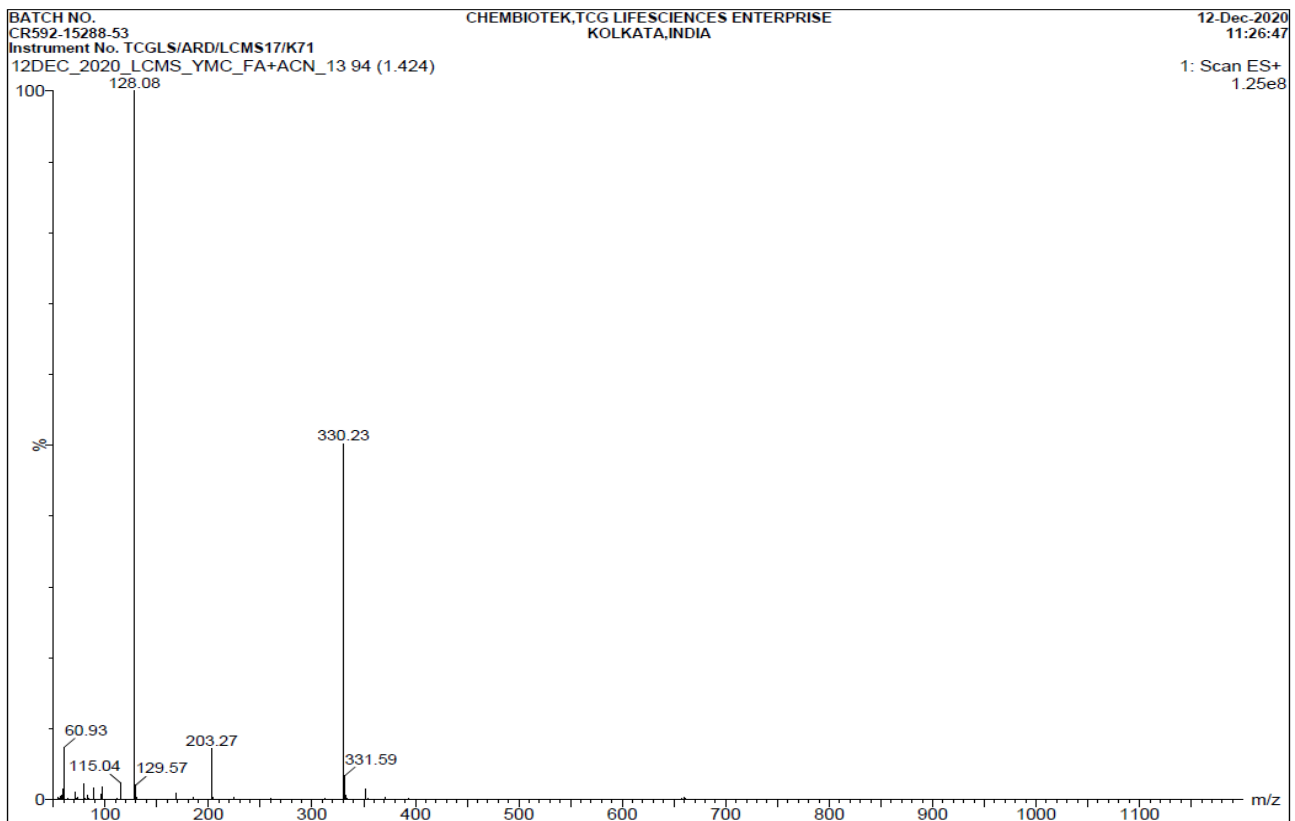
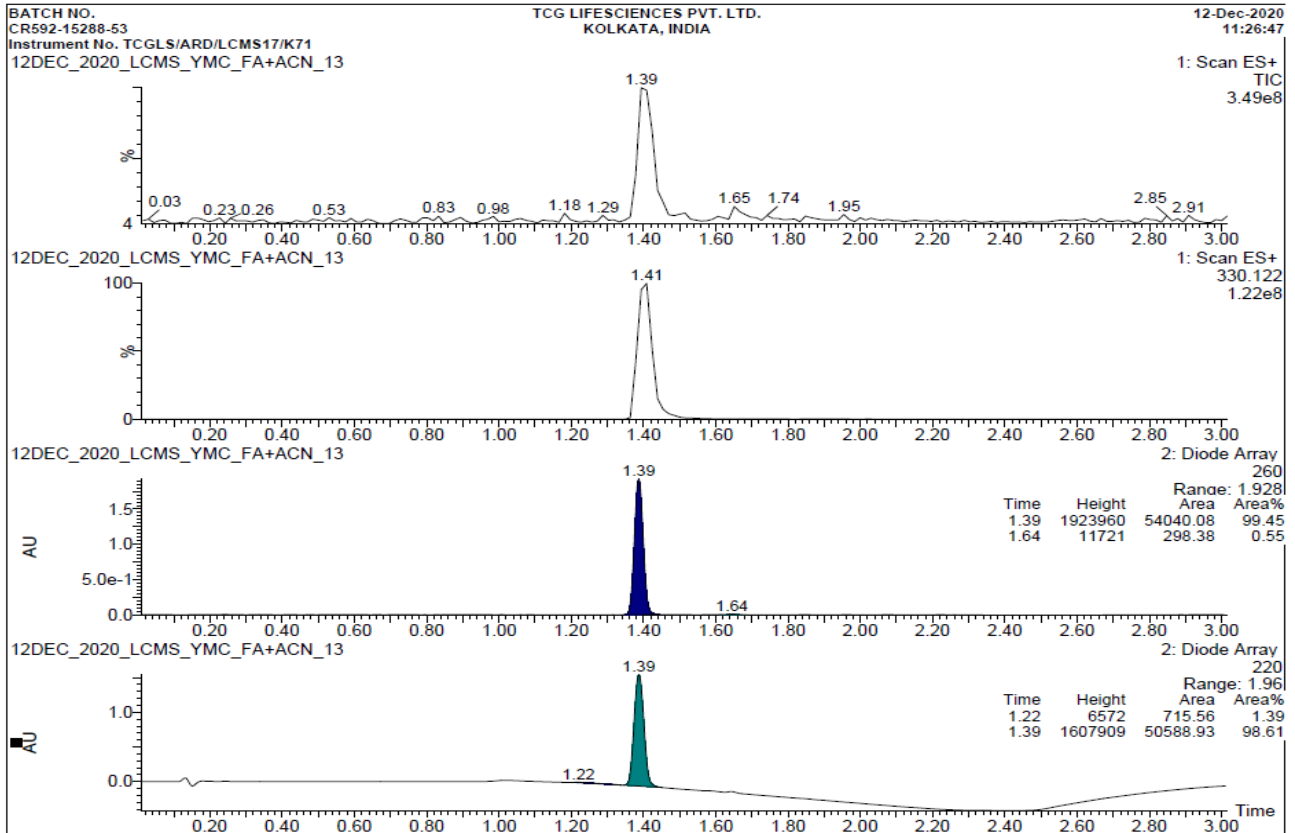
Attachment-28-1HNMR



Attachment-29-13CNMR

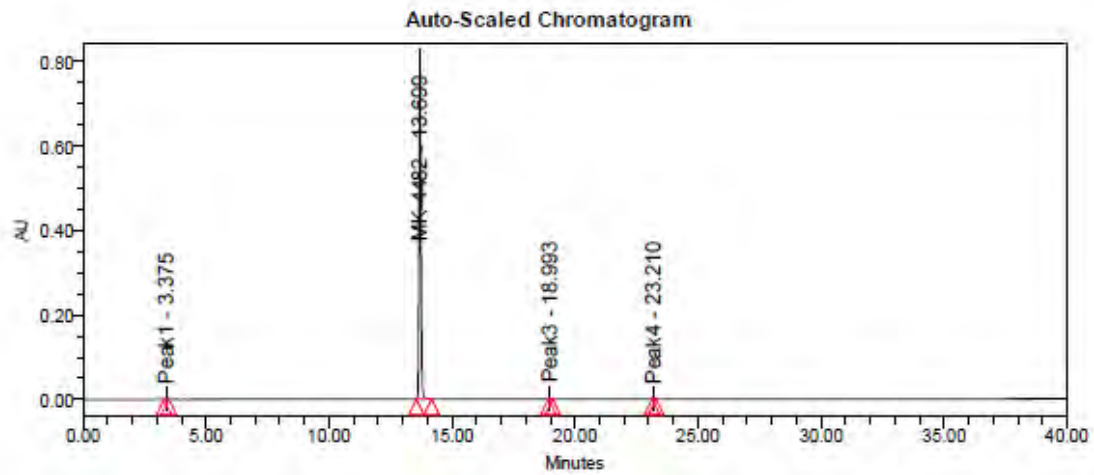


Attachment-30-LCMS



Attachment-31-HPLC

SAMPLE INFORMATION			
Sample Name:	CR592-15288-03	Acquired By:	PG0112811
Sample Type:	Unknown	Sample Set Name:	TCGLS_111220A
Vial:	46	Acq. Method Set:	EIDD_2801_OPA
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 260.0 nm (2998)
Date Acquired:	11-12-2020 23:04:09 IST	Column Name:	XTERRA RP18 (250*4.6) mm, 5µ
Date Processed:	12-12-2020 10:38:45 IST		

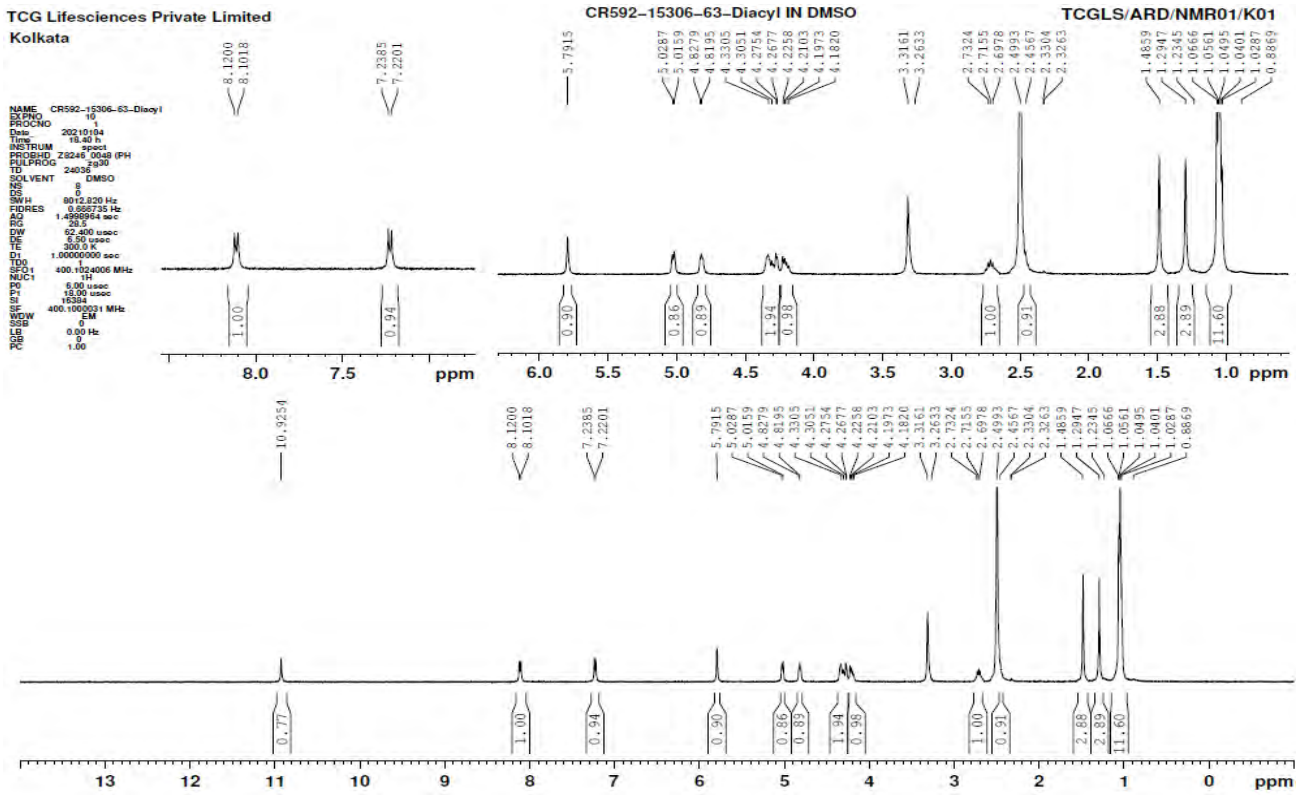


Peak Results					
	Name	RT	Area	% Area	RT Ratio
1	Peak1	3.375	5605	0.14	0.248
2	MK-4482	13.699	4053891	99.67	1.000
3	Peak3	18.993	7201	0.18	1.386
4	Peak4	23.210	795	0.02	1.694

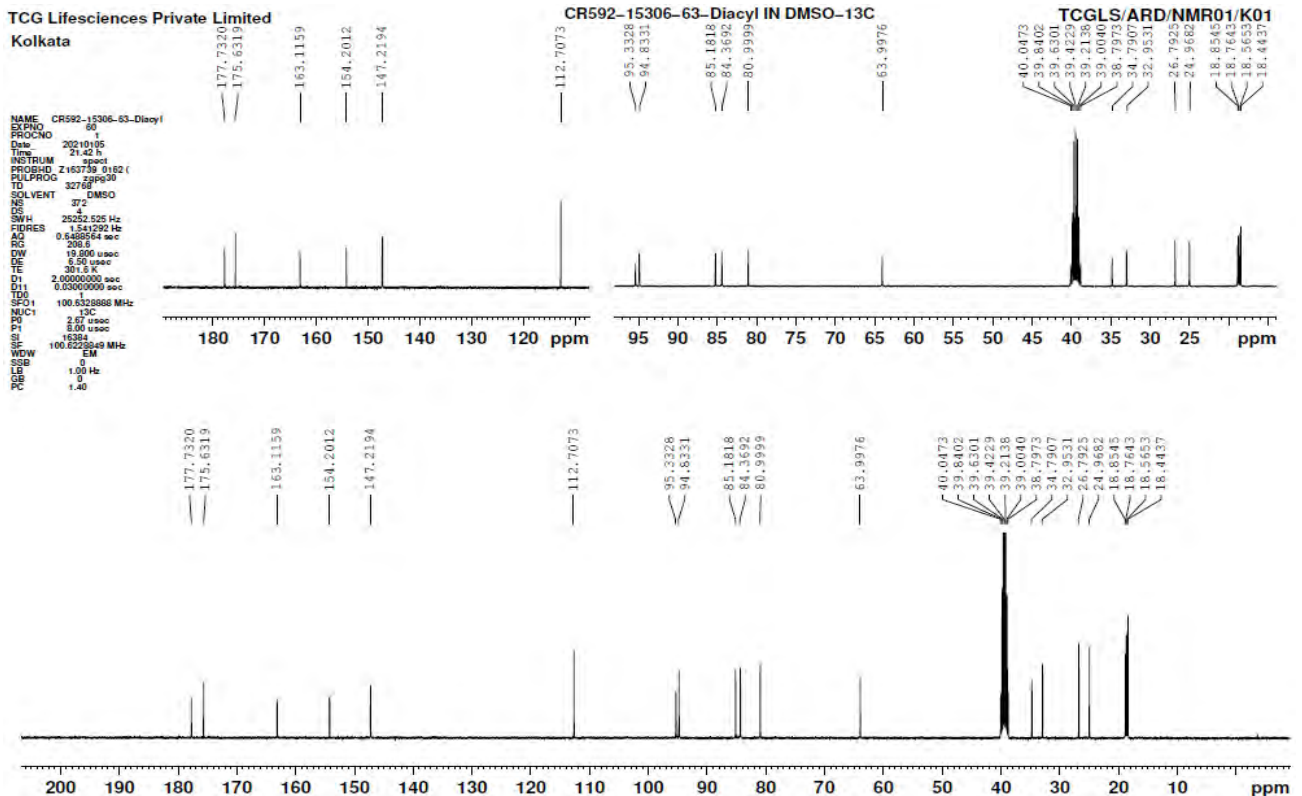
Reported by User: Partha Sarathi Ghosh (PG0112811)
 Report Method: TCGLS_Report
 Report Method ID: 25877
 Page: 1 of 1

Project Name: QCHPLC042
 Date Printed: 12-12-2020
 10:40:41 Asia/Kolkata

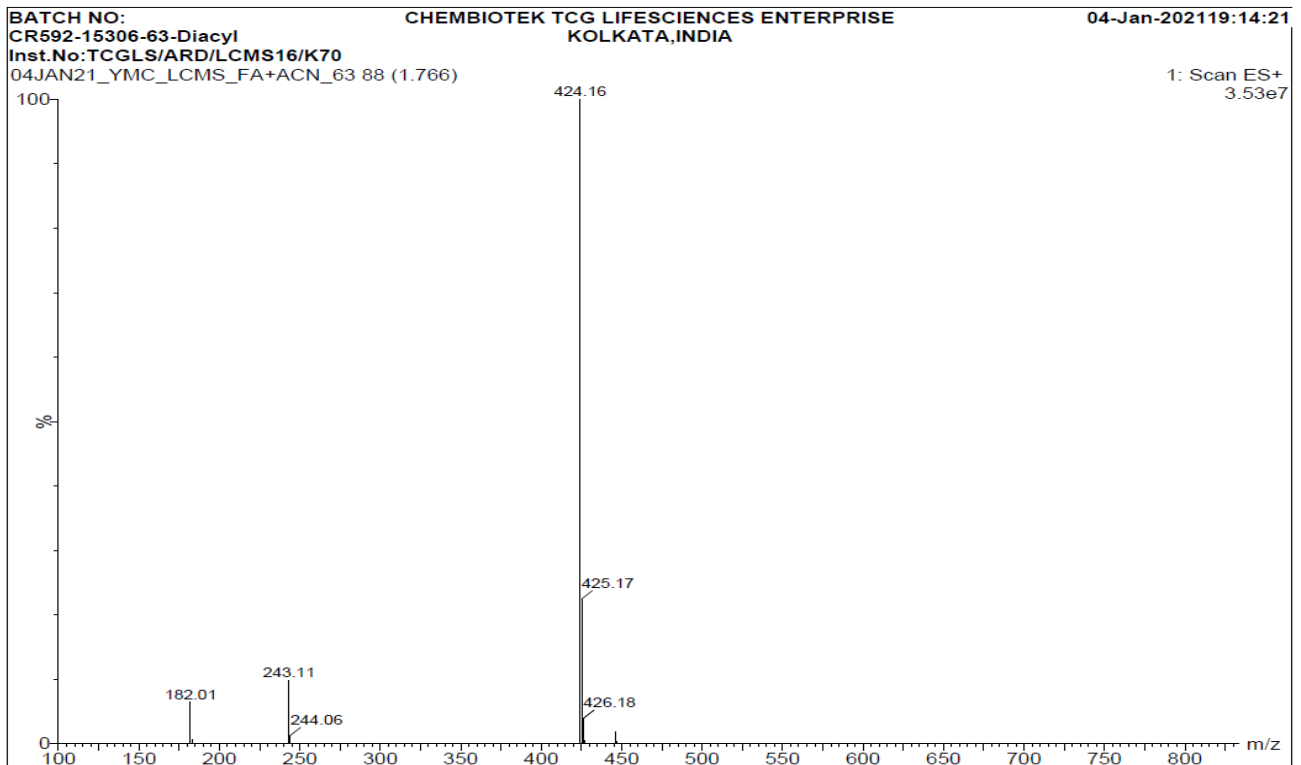
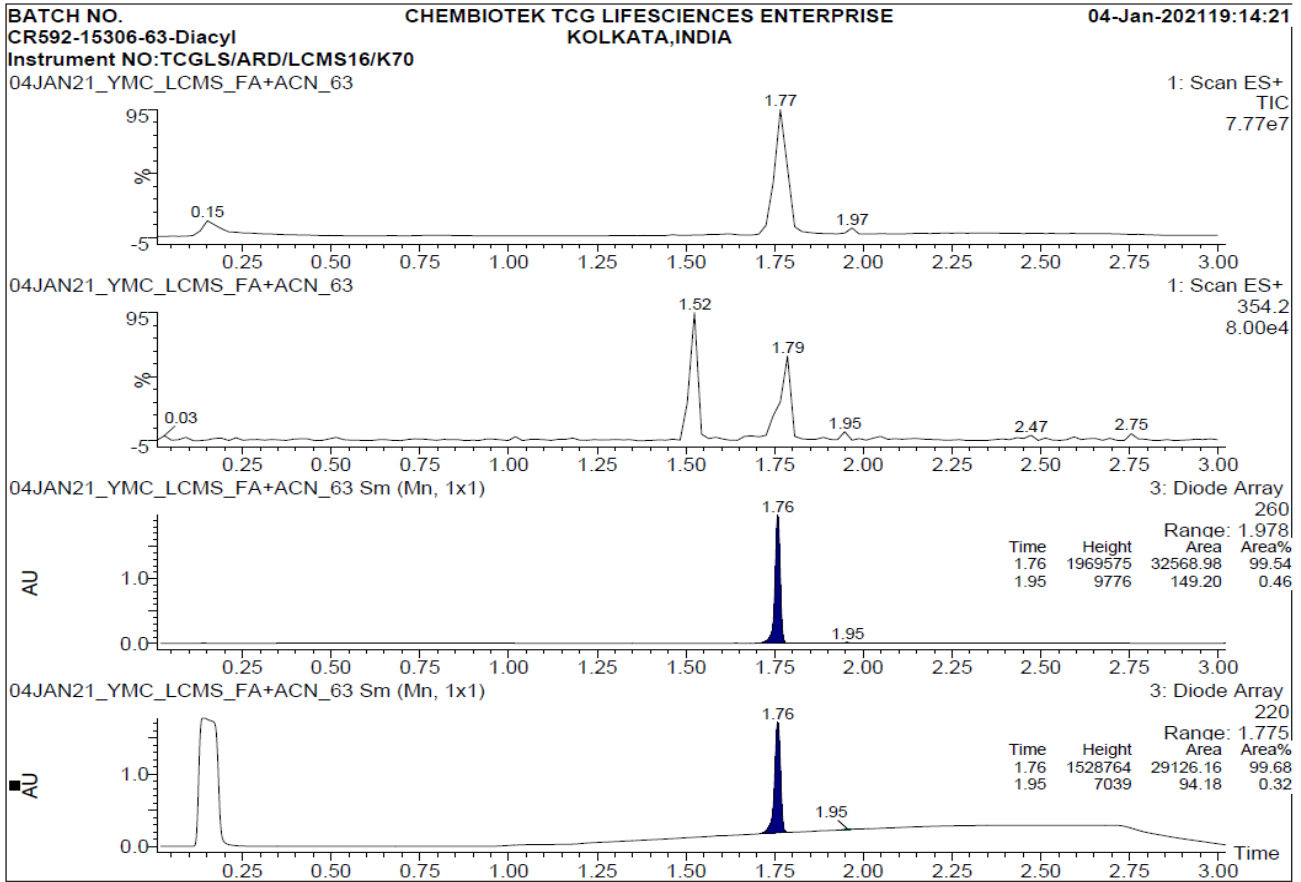
Attachment-32-1HNMR



Attachment-33-13CNMR

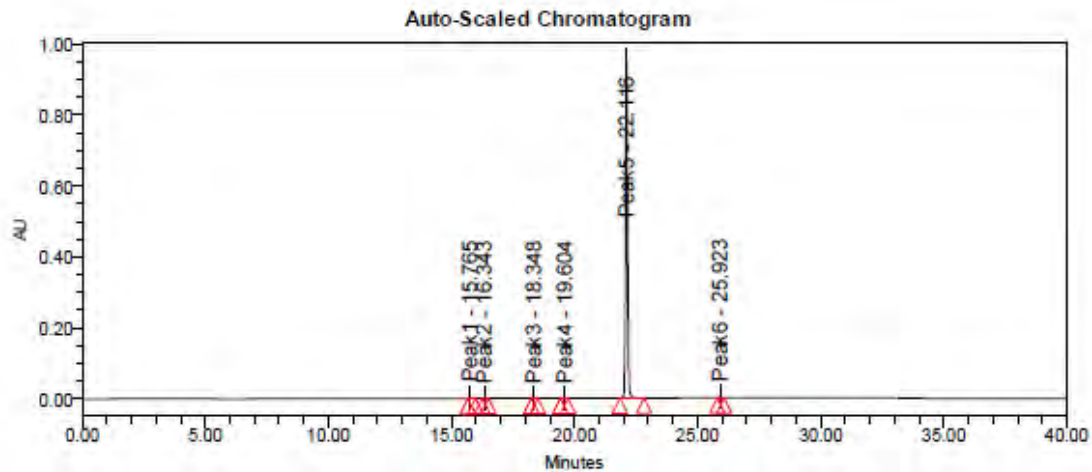


Attachment-34-LCMS



Attachment-35-HPLC

SAMPLE INFORMATION			
Sample Name:	CR552-15306-E3-Diacyl	Acquired By:	AM0113345
Sample Type:	Unknown	Sample Set Name:	TCGLS_010121
Vial:	3	Acq. Method Set:	EIDD_2801_OPA
Injection #:	1	Processing Method:	EIDD_1
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 260.0 nm (2998)
Date Acquired:	04-01-2021 19:21:00 IST	Column Name:	XTERRA RP 18 (250x4.6)5u
Date Processed:	04-01-2021 20:36:36 IST		



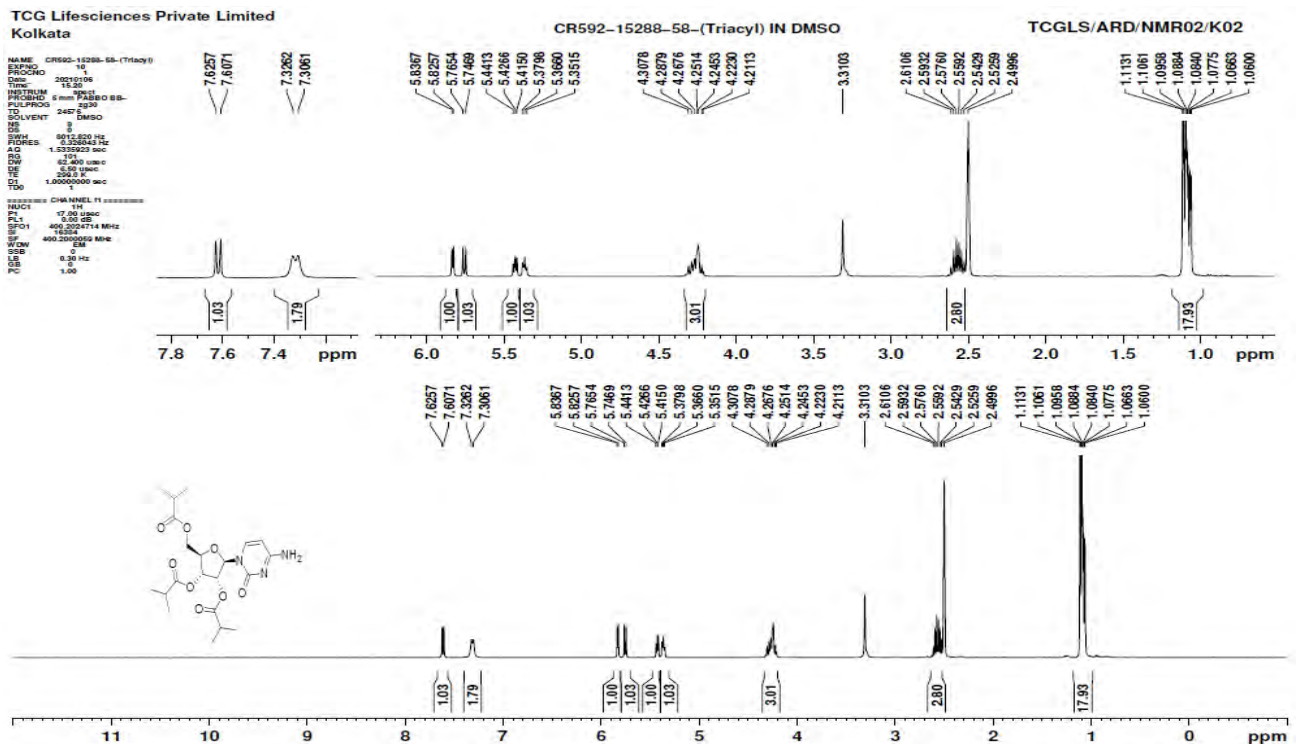
Peak Results

Name	RT	Area	% Area	RT Ratio
1 Peak1	15.765	9963	0.19	0.713
2 Peak2	16.343	1972	0.04	0.739
3 Peak3	18.348	1673	0.03	0.830
4 Peak4	19.604	2703	0.05	0.886
5 Peak5	22.116	5220566	99.25	1.000
6 Peak6	25.923	22989	0.44	1.172

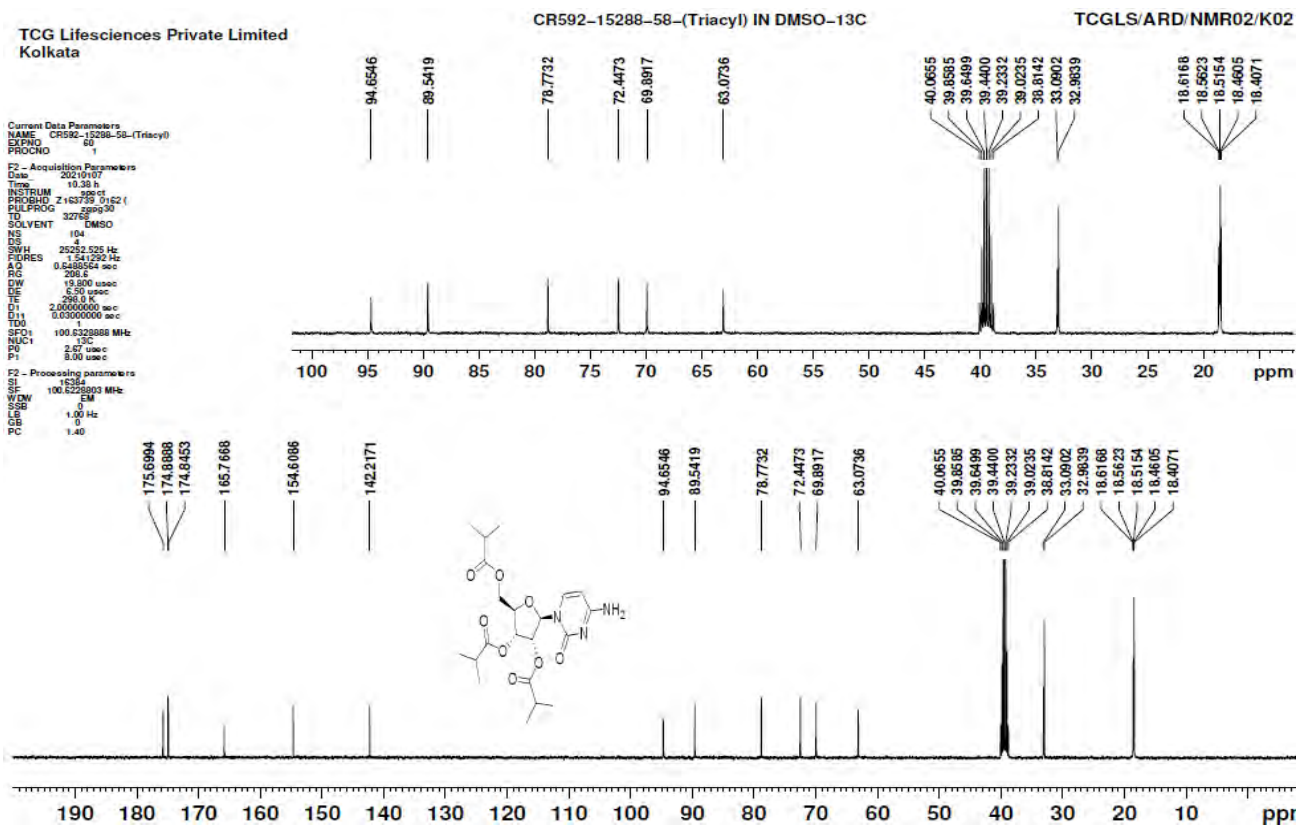
Reported by User: Soumen Pramanik (SP0113317)
 Report Method: TCGLS_Report
 Report Method ID: 46214
 Page: 1 of 1

Project Name: QCHPLC042
 Date Printed: 04-01-2021
 20:37:26 Asia/Kolkata

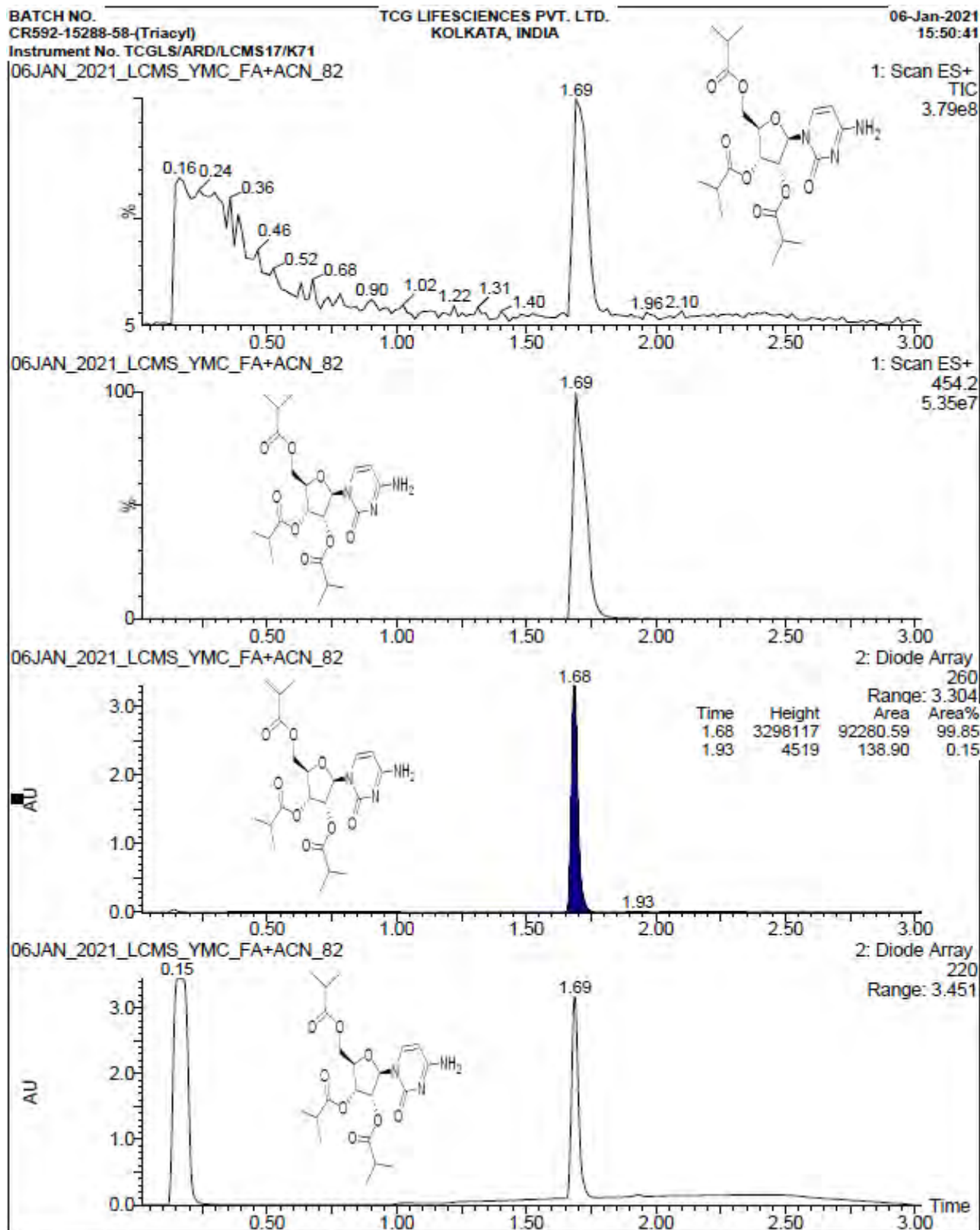
Attachment-36-1HNMR



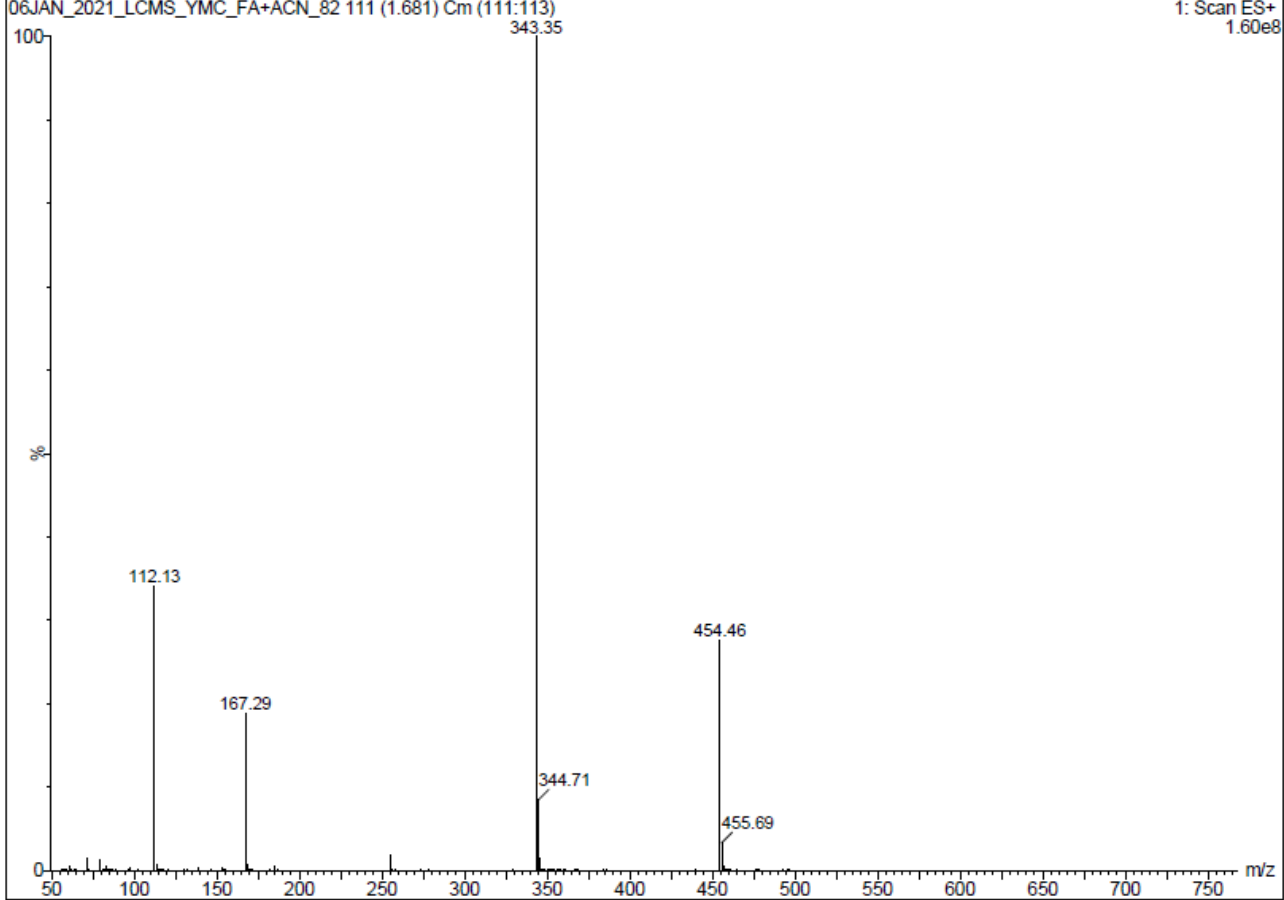
Attachment-37-13CNMR



Attachment-38-LCMS



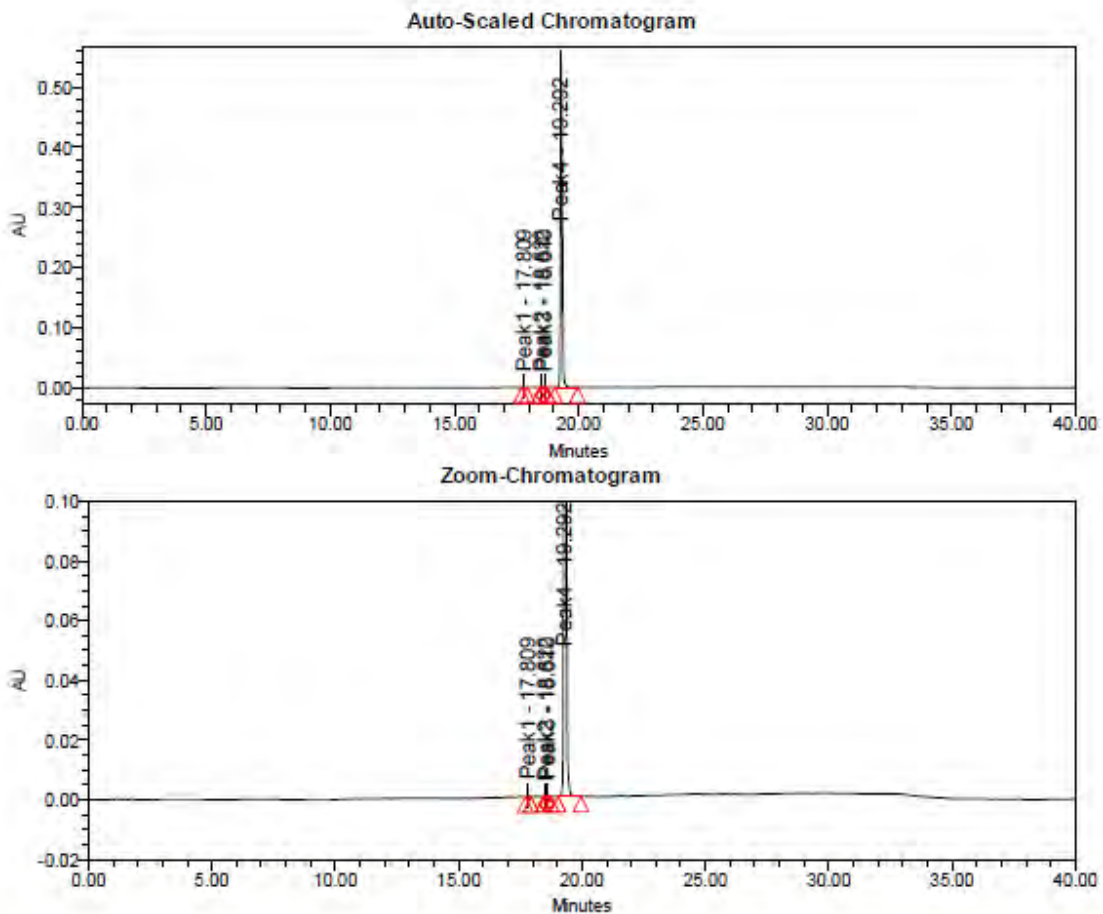
BATCH NO. CHEMBIOTEK,TCG LIFESCIENCES ENTERPRISE 06-Jan-2021
CR592-15288-58-(Triacyl) KOLKATA,INDIA 15:50:41
Instrument No. TCGLS/ARD/LCMS17/K71
06JAN_2021_LCMS_YMC_FA+ACN_82 111 (1.681) Cm (111:113) 1: Scan ES+
1.60e8



Attachment-39-HPLC

TCGLS Report ZOOM

SAMPLE INFORMATION			
Sample Name:	CR552-15288-98-(Triacyl)	Acquired By:	AMD113345
Sample Type:	Unknown	Sample Set Name:	TCGLS_060121
Vial:	40	Acq. Method Set:	EIDD_2801_OPA
Injection #:	1	Processing Method:	EIDD_1
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 260.0 nm (2998)
Date Acquired:	06-01-2021 16:50:10 IST	Column Name:	XTERRA RP 18 (250X4.6)5u
Date Processed:	06-01-2021 17:39:18 IST		



Reported by User: Sandip Shyam (SS0113466)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 50929
 Page: 1 of 2

Project Name: QCHPLC042
 Date Printed: 06-01-2021
 17:39:57 Asia/Kolkata

Peak Results

	Name	RT	Area	% Area	RT Ratio
1	Peak1	17.809	1800	0.07	0.923
2	Peak2	18.522	990	0.04	0.960
3	Peak3	18.610	1589	0.06	0.965
4	Peak4	19.292	2713667	99.84	1.000

Reported by User: Sandip Shyam (SS0113466)
Report Method: TCGLS_Report_ZOOM
Report Method ID: 50929
Page: 2 of 2

Project Name: QCHPLC042
Date Printed:
06-01-2021
17:39:57 Asia/Kolkata

Attachment-40-1HNMR

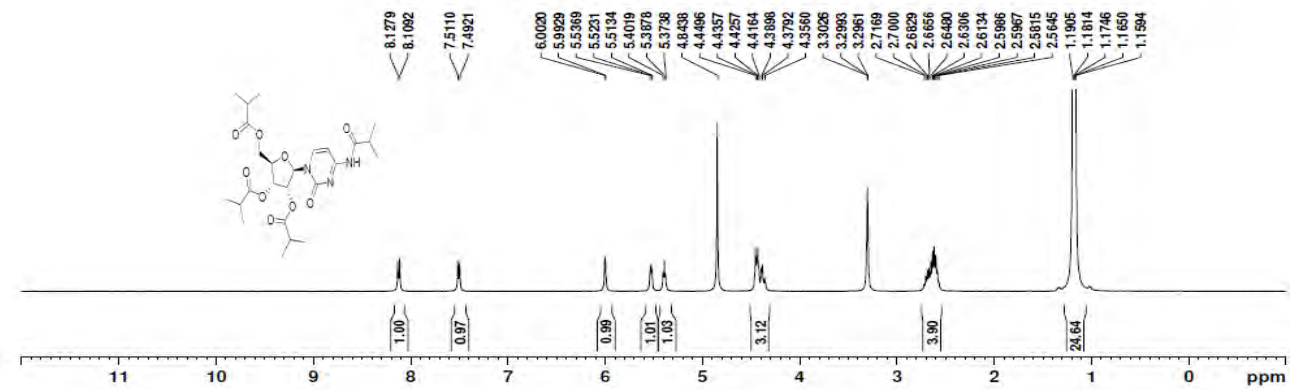
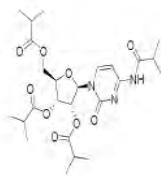
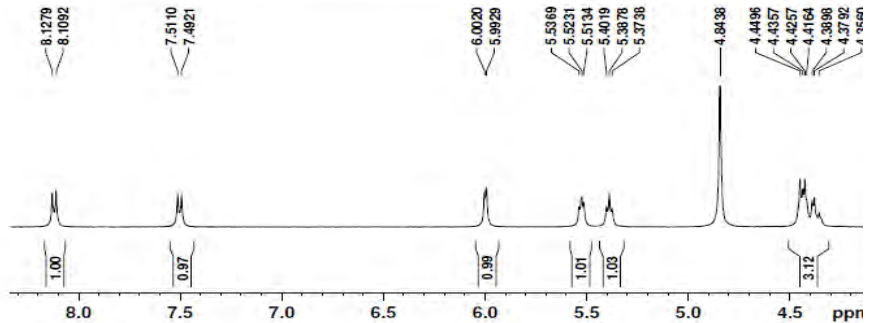
TCG Lifesciences Private Limited
Kolkata

CR592-15288-58-F1-(tetraacyl) IN MeOD

TCGLS/ARD/NMR01/K01

```

NAME CR592-15288-58-F1-(tetraacyl)
EXPNO 15
PROCNO 1
Date_ 20210106
Time 13:32 h
INSTRUM spect
PROBHD ZS244-0041 PH
PULPROG zgpg30
SOLVENT MeOD
NS 8
DS 4
SWH 8012.820 Hz
F2 - Acquisition Parameters
F2RES 1.656736 Hz
AQ 1.4026964 sec
RG 403
DW 62.400 usec
DE 5.81 usec
TE 300.2 K
D1 1.0000000 sec
TD0
SFO1 400.1504006 MHz
NUC1 13C
PC 1
P1 6.00 usec
SF 100.6261157 MHz
DEWB 0
SFB 0
GB 0
PC 1.00
    
```



Attachment-41-13CNMR

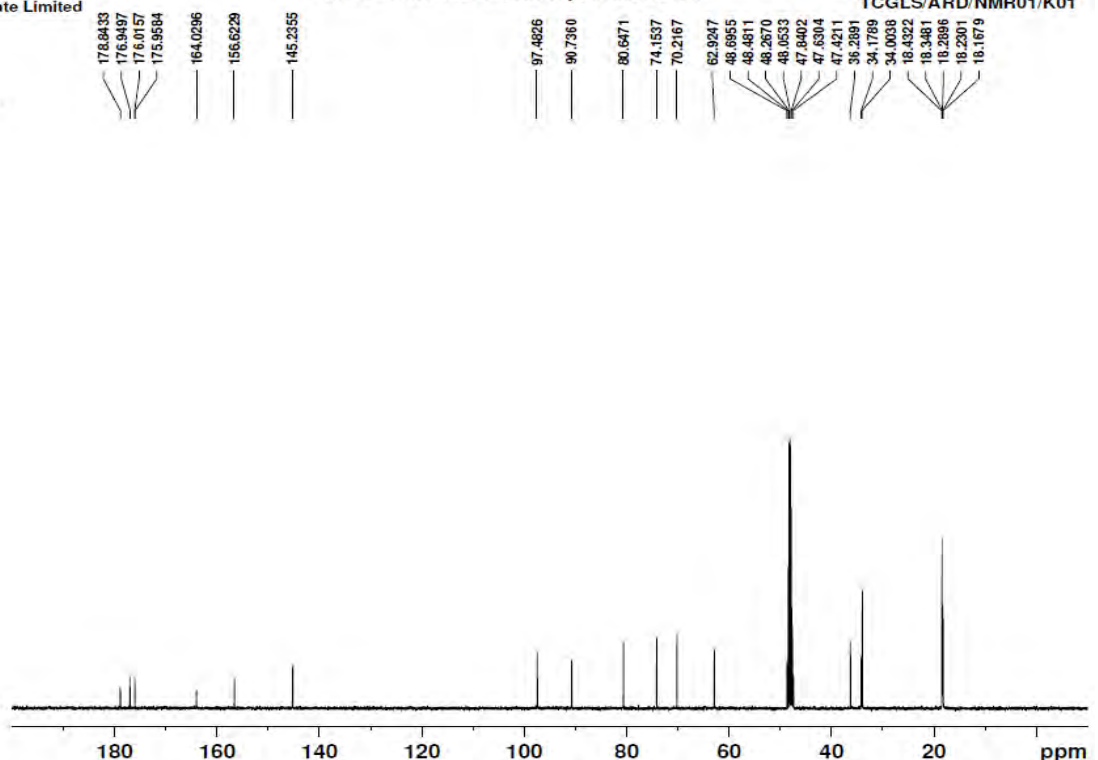
TCG Lifesciences Private Limited
Kolkata

CR592-15288-58-F1-(tetra acyl) IN MeOD-13C

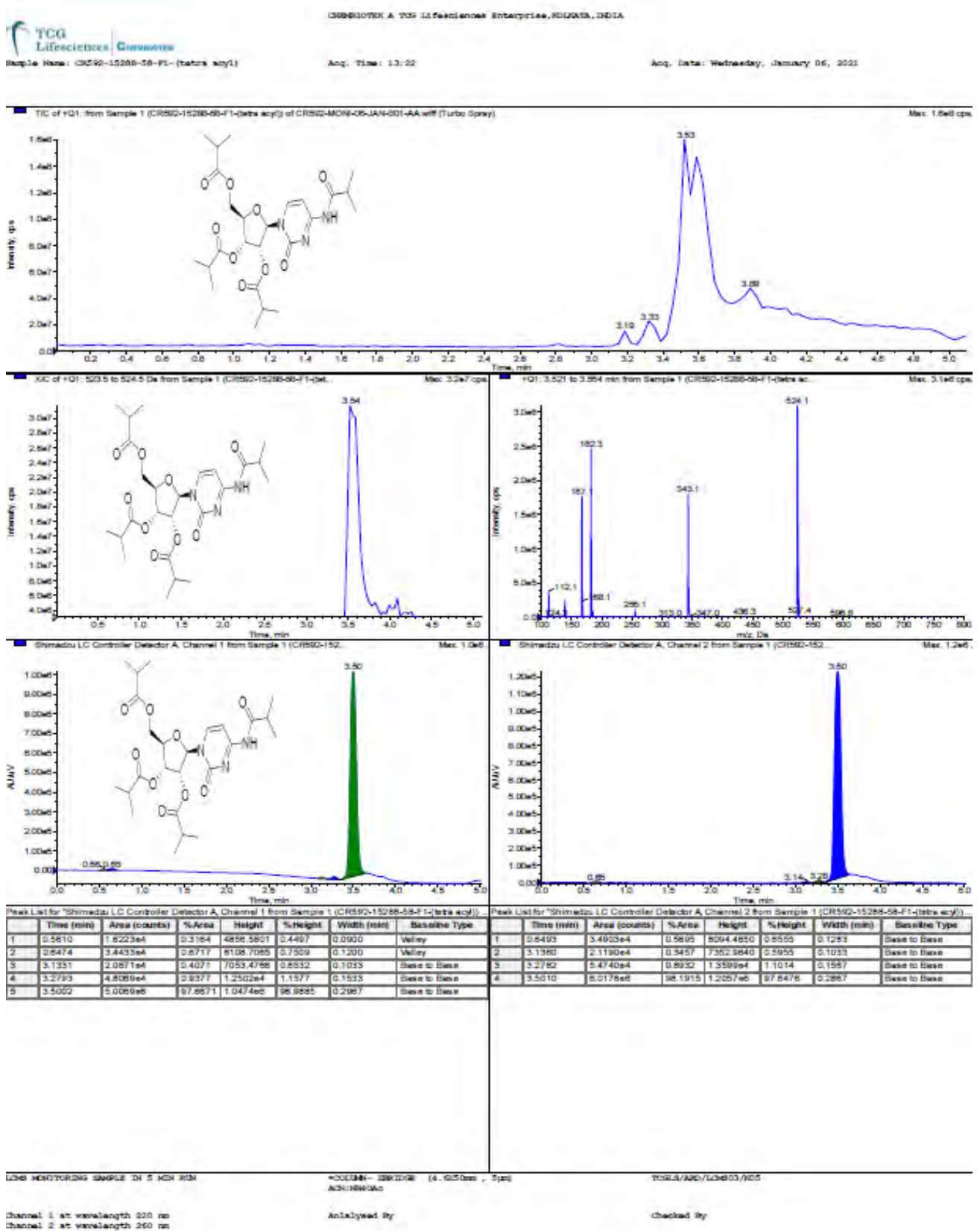
TCGLS/ARD/NMR01/K01

```

Current Data Parameters
NAME CR592-15288-58-F1-(tetra acyl)
EXPNO 60
PROCNO 1
F2 - Acquisition Parameters
Date_ 20210106
Time 13:16 h
INSTRUM spect
PROBHD Z163759 0152 (
PULPROG zgpg30
SOLVENT MeOD
NS 150
DS 4
SWH 25254.525 Hz
F2RES 174.1292 Hz
AQ 0.6480964 sec
RG 209.5
DW 19.500 usec
DE 5.50 usec
TE 300.2 K
D1 1.0000000 sec
D11 0.0300000 sec
TD0
SFO1 100.626888 MHz
NUC1 13C
PC 1
P1 2.67 usec
SF 100.622340 MHz
F2 - Processing parameters
SI 16384
SF 100.622340 MHz
WDW 0
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
    
```



Attachment-42-LCMS

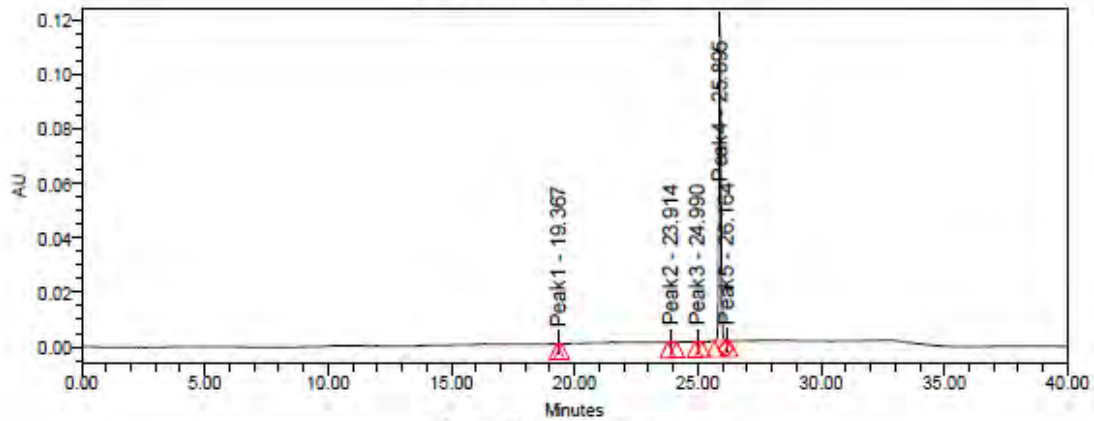


Attachment-43-HPLC

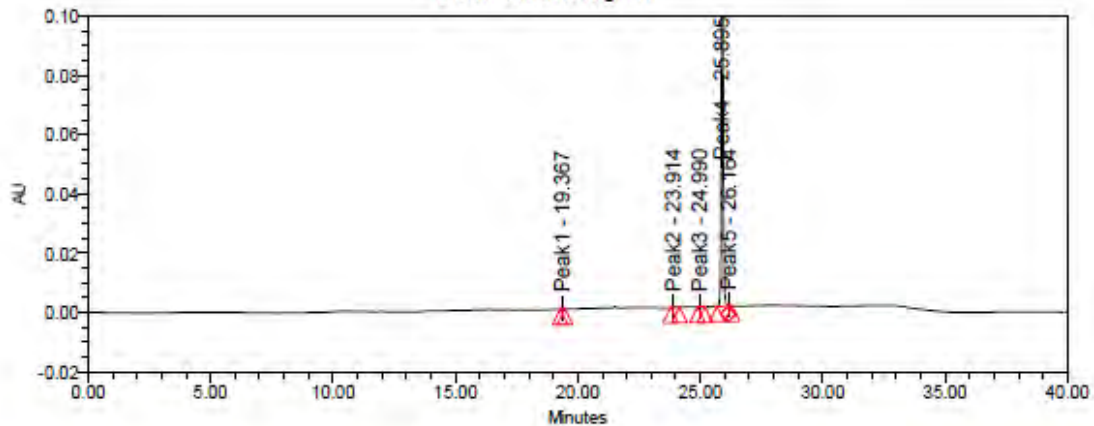
TCGLS Report ZOOM

SAMPLE INFORMATION			
Sample Name:	CR592-15286-88-F11 (Tetra-oc)	Acquired By:	AM0113345
Sample Type:	Unknown	Sample Set Name:	TCGLS_060121
Vial:	36	Acq. Method Set:	EIDD_2801_OPA
Injection #:	1	Processing Method:	EIDD_1
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 260.0 nm (2998)
Date Acquired:	06-01-2021 13:19:58 IST	Column Name:	XTERRA RP 18 (250x4.6)5u
Date Processed:	06-01-2021 14:48:52 IST		

Auto-Scaled Chromatogram



Zoom-Chromatogram



Reported by User: Sandip Shyam (SS0113466)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 50929
 Page: 1 of 2

Project Name: QCHPLC042
 Date Printed: 06-01-2021
 14:49:52 Asia/Kolkata

Peak Results

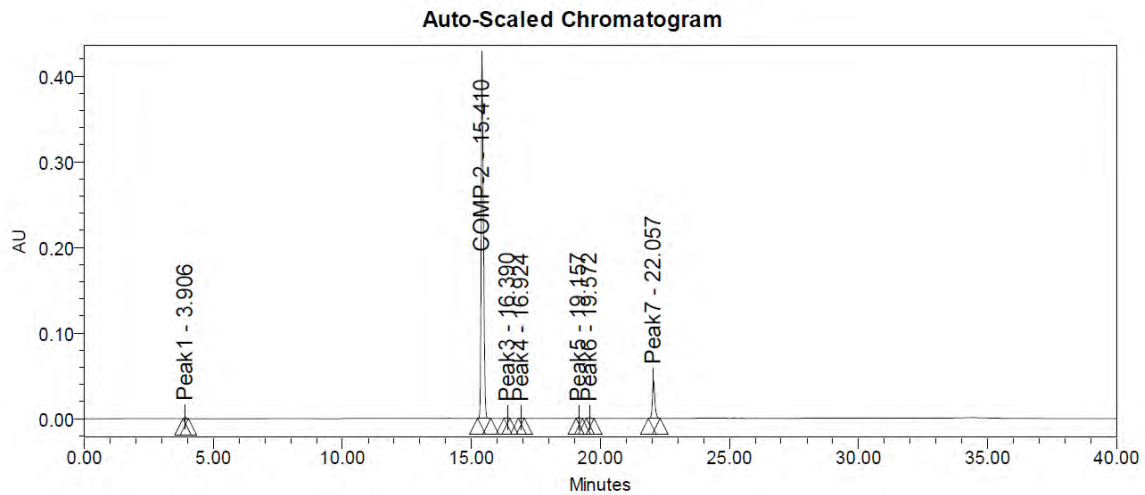
	Name	RT	Area	% Area	RT Ratio
1	Peak1	19.367	1451	0.23	0.748
2	Peak2	23.914	2233	0.35	0.924
3	Peak3	24.990	1328	0.21	0.965
4	Peak4	25.895	636500	98.98	1.000
5	Peak5	26.164	1520	0.24	1.010

Reported by User: Sandip Shyam (SS0113466)
Report Method: TCGLS_Report_ZOOM
Report Method ID: 50929
Page: 2 of 2

Project Name: QCHPLC042
Date Printed:
06-01-2021
14:49:52 Asia/Kolkata

Attachment-44-HPLC

SAMPLE INFORMATION			
Sample Name:	CR592-16022-89-P	Acquired By:	SP0113317
Sample Type:	Unknown	Sample Set Name:	TCGLS_210621A
Vial:	14	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 260.0 nm (2998)
Date Acquired:	21-06-2021 23:52:07 IST	Column Name:	XTERRA RP18(250X4.6)mm,5µ
Date Processed:	22-06-2021 06:29:38 IST		



Peak Results

	Name	RT	Area	% Area	RT Ratio
1	Peak1	3.906	9008	0.31	0.254
2	COMP-2	15.410	2578138	88.95	1.000
3	Peak3	16.390	4057	0.14	1.064
4	Peak4	16.924	1901	0.07	1.098
5	Peak5	19.157	5375	0.19	1.243
6	Peak6	19.572	6721	0.23	1.270
7	Peak7	22.057	293109	10.11	1.431

Reported by User: Soumya chatterjee (SC0113139)
 Report Method: TCGLS_Report
 Report Method ID: 83008
 Page: 1 of 1

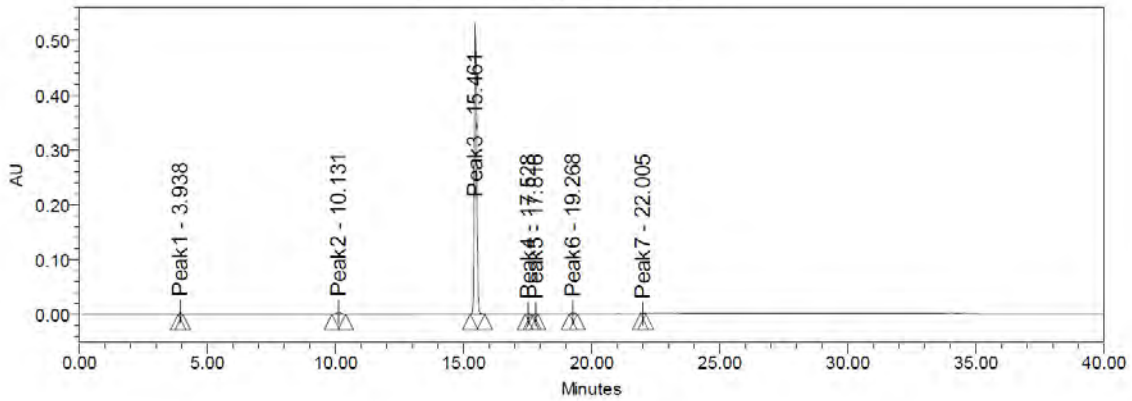
Project Name: QCHPLC041
 Date Printed: 22-06-2021
 06:39:49 Asia/Kolkata

Attachment-45-HPLC

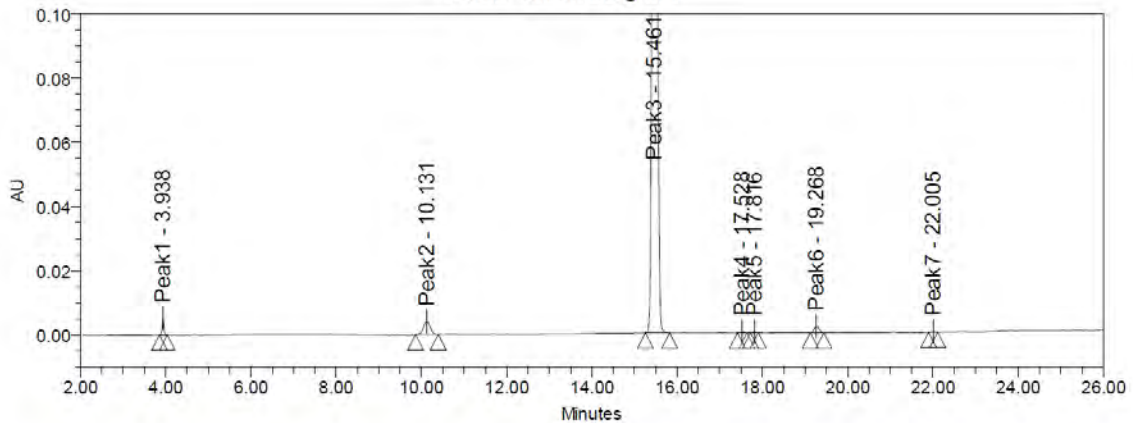
TCGLS_Report_ZOOM

SAMPLE INFORMATION			
Sample Name:	CR592-16492-21-P	Acquired By:	SS0113466
Sample Type:	Unknown	Sample Set Name:	TCGLS_130721
Vial:	63	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 260nm@4.8nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 260nm@4.8nm
Date Acquired:	14-07-2021 05:35:25 IST	Column Name:	XTERRA RP18(250X4.6)mm,5µ
Date Processed:	14-07-2021 09:23:42 IST		

Auto-Scaled Chromatogram



Zoom - Chromatogram



Reported by User: Sandip Shyam (SS0113466)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 89512
 Page: 1 of 2

Project Name: QCHPLC041
 Date Printed: 14-07-2021
 09:25:16 Asia/Kolkata

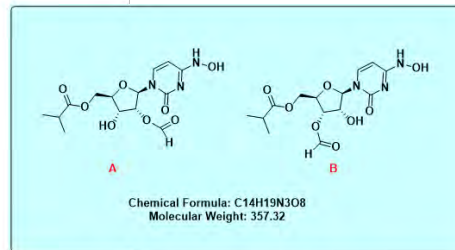
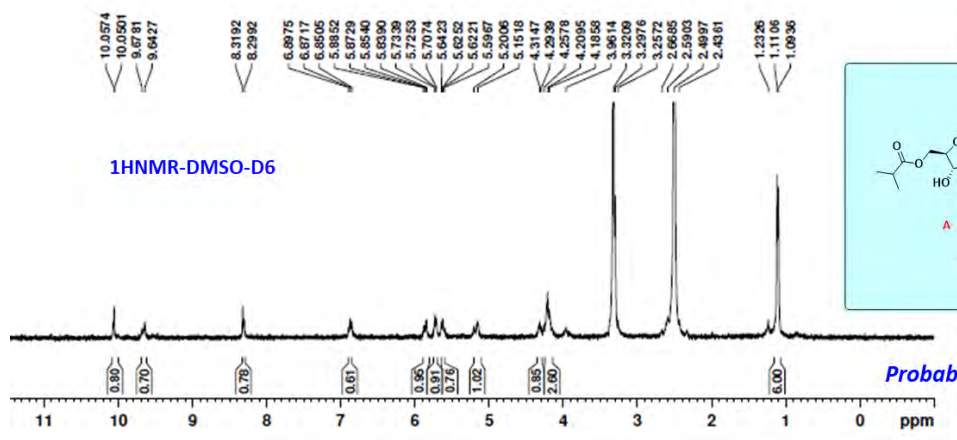
Peak Results

	Name	RT	Area	% Area	RT Ratio
1	Peak1	3.938	14326	0.42	0.25
2	Peak2	10.131	44509	1.32	0.66
3	Peak3	15.461	3293611	97.67	1.00
4	Peak4	17.528	2042	0.06	1.13
5	Peak5	17.816	1006	0.03	1.15
6	Peak6	19.268	15392	0.46	1.25
7	Peak7	22.005	1466	0.04	1.42

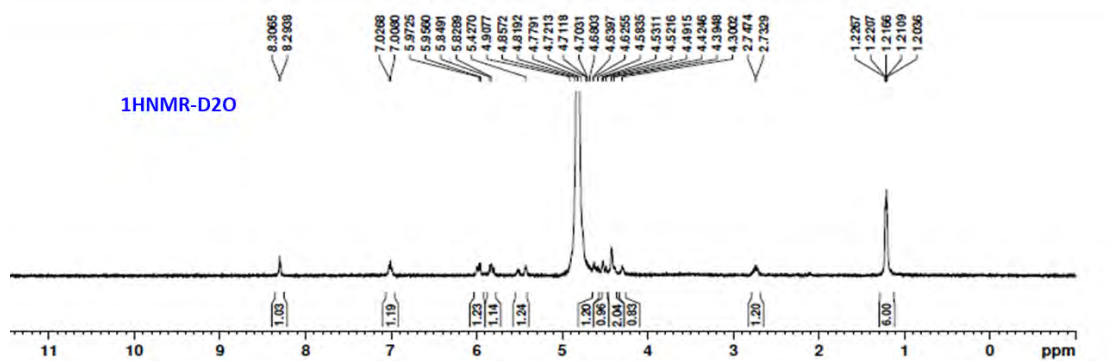
Reported by User: Sandip Shyam (SS0113466)
Report Method: TCGLS_Report_ZOOM
Report Method ID: 89512
Page: 2 of 2

Project Name: QCHPLC041
Date Printed:
14-07-2021
09:25:16 Asia/Kolkata

Attachment-46-1HNMR



Probable structures of the impurities

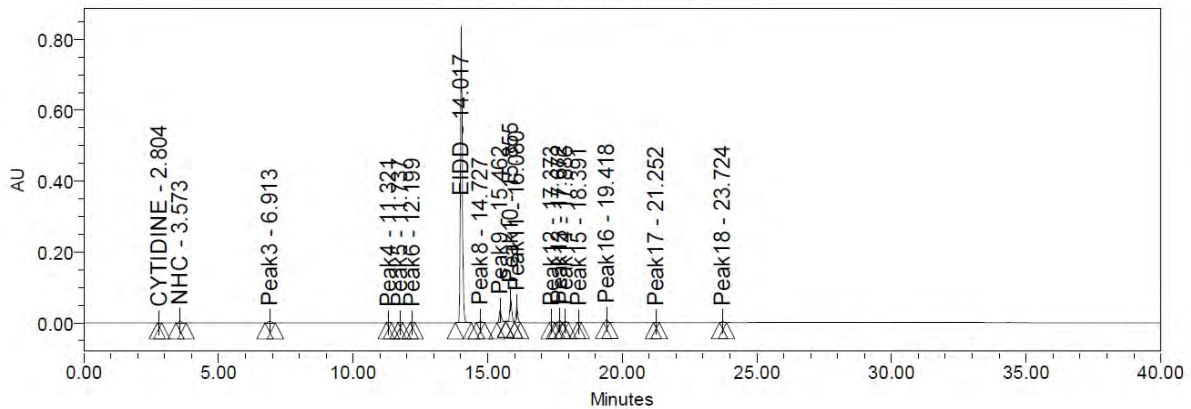


Attachment-47-HPLC

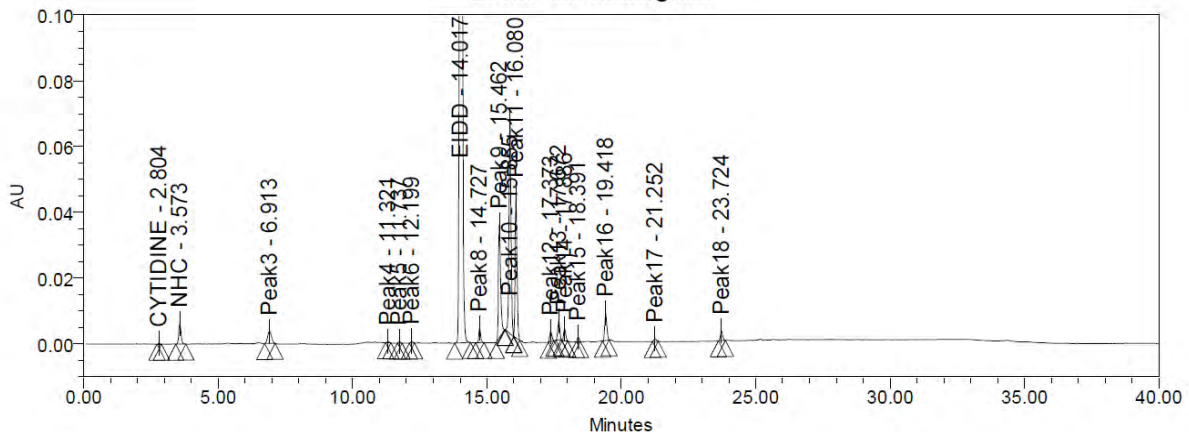
TCGLS_Report_ZOOM

SAMPLE INFORMATION			
Sample Name:	CR592-16306-85-CR	Acquired By:	AM0113345
Sample Type:	Unknown	Sample Set Name:	TCGLS_010621
Vial:	33	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 260.0 nm (2998)
Date Acquired:	01-06-2021 19:55:50 IST	Column Name:	XTERRA RP18(250X4.6)mm,5µ
Date Processed:	02-06-2021 13:36:04 IST		

Auto-Scaled Chromatogram



Zoom- Chromatogram



Reported by User: Sandip Shyam (SS0113466)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 72940
 Page: 1 of 2

Project Name: QCHPLC041
 Date Printed: 02-06-2021
 13:36:56 Asia/Kolkata

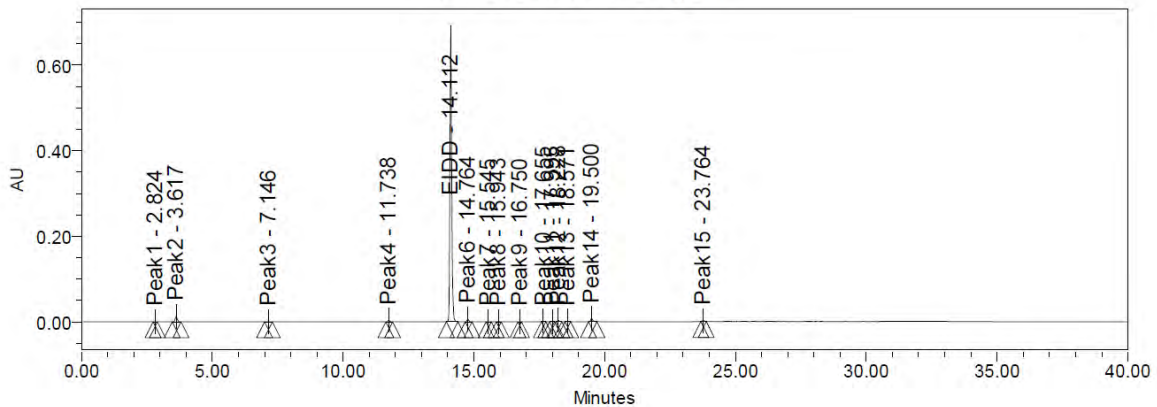
Peak Results

	Name	RT	Area	% Area	RT Ratio
1	CYTIDINE	2.804	1299	0.03	0.20
2	NHC	3.573	37095	0.74	0.25
3	Peak3	6.913	37469	0.75	0.49
4	Peak4	11.321	2436	0.05	0.81
5	Peak5	11.737	2524	0.05	0.84
6	Peak6	12.199	2906	0.06	0.87
7	EIDD	14.017	3998586	80.10	1.00
8	Peak8	14.727	21396	0.43	1.05
9	Peak9	15.462	191147	3.83	1.10
10	Peak10	15.855	342400	6.86	1.13
11	Peak11	16.080	212984	4.27	1.15
12	Peak12	17.373	16774	0.34	1.24
13	Peak13	17.672	31266	0.63	1.26
14	Peak14	17.886	20687	0.41	1.28
15	Peak15	18.391	6199	0.12	1.31
16	Peak16	19.418	45384	0.91	1.39
17	Peak17	21.252	4833	0.10	1.52
18	Peak18	23.724	16695	0.33	1.69

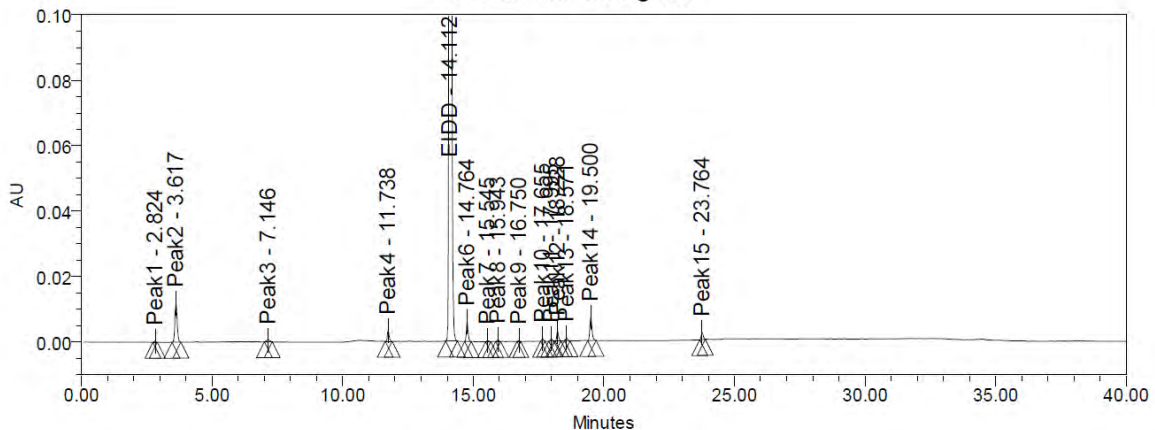
Attachment-48-HPLC

SAMPLE INFORMATION			
Sample Name:	CR592-16306-85-CR-24h	Acquired By:	SP0113317
Sample Type:	Unknown	Sample Set Name:	TCGLS_030621
Vial:	5	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 260.0 nm (2998)
Date Acquired:	03-06-2021 11:15:53 IST	Column Name:	XTERRA RP18(250X4.6)mm,5µ
Date Processed:	03-06-2021 12:08:33 IST		

Auto-Scaled Chromatogram



Zoom- Chromatogram



Reported by User: Soumen Pramanik (SP0113317)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 72940
 Page: 1 of 2

Project Name: QCHPLC041
 Date Printed: 03-06-2021
 12:09:16 Asia/Kolkata

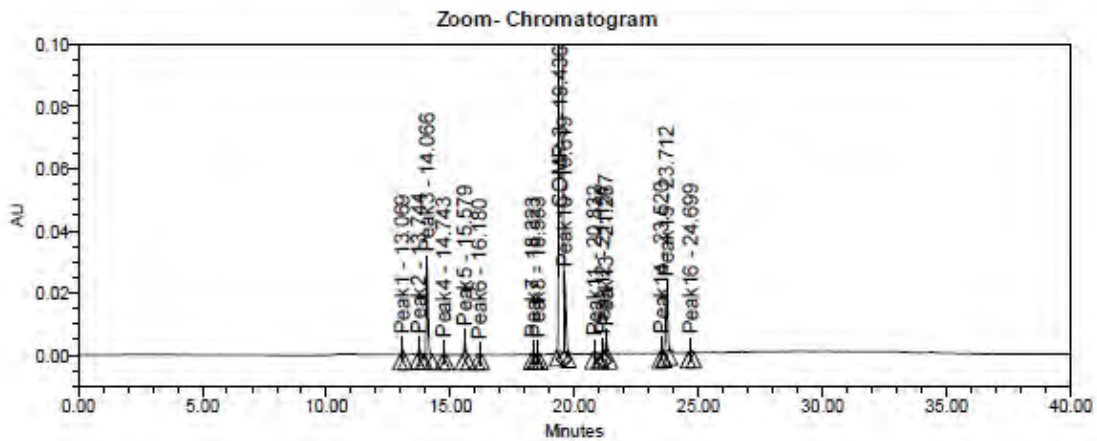
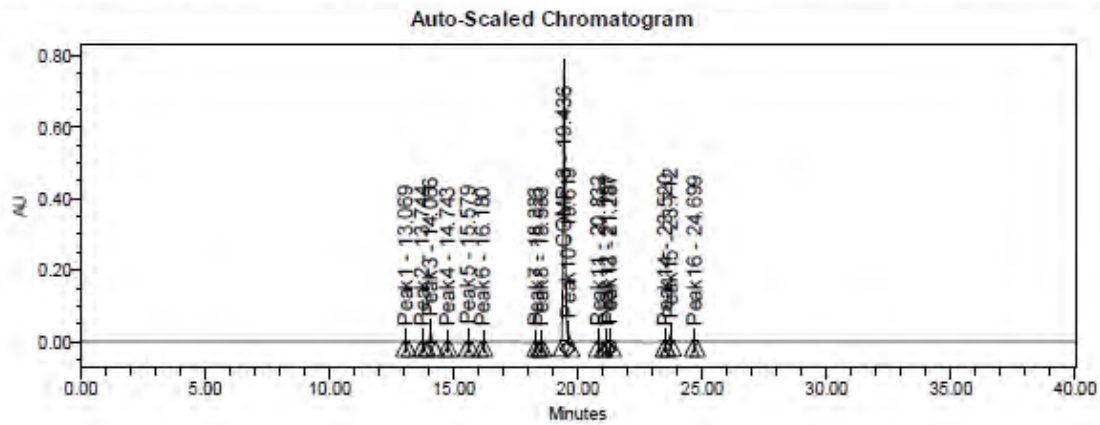
Peak Results

	Name	RT	Area	% Area	RT Ratio
1	Peak1	2.824	1741	0.05	0.20
2	Peak2	3.617	72648	2.14	0.26
3	Peak3	7.146	5064	0.15	0.51
4	Peak4	11.738	15619	0.46	0.83
5	EIDD	14.112	3183218	93.93	1.00
6	Peak6	14.764	28458	0.84	1.05
7	Peak7	15.545	1848	0.05	1.10
8	Peak8	15.943	2906	0.09	1.13
9	Peak9	16.750	1018	0.03	1.19
10	Peak10	17.655	3403	0.10	1.25
11	Peak11	17.995	3108	0.09	1.28
12	Peak12	18.228	14260	0.42	1.29
13	Peak13	18.571	4134	0.12	1.32
14	Peak14	19.500	40203	1.19	1.38
15	Peak15	23.764	11279	0.33	1.68

Attachment-49-HPLC

TCGLS Report ZOOM

SAMPLE INFORMATION			
Sample Name:	CR992-18022-62-Cr	Acquired By:	AM0113345
Sample Type:	Unknown	Sample Set Name:	TCGLS_030621
Vial:	15	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 260.0 nm (2998)
Date Acquired:	03-06-2021 21:30:50 IST	Column Name:	XTERRA RP18(250X4.6)mm,5µ
Date Processed:	04-06-2021 07:57:38 IST		



Reported by User: Partha Pratim Bal (PB0112721)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 72940
 Page: 1 of 2

Project Name: QCHPLC041
 Date Printed: 04-06-2021
 07:57:59 Asia/Kolkata

Peak Results

	Name	RT	Area	% Area	RT Ratio
1	Peak1	13.069	8739	0.19	0.67
2	Peak2	13.744	8820	0.19	0.71
3	Peak3	14.066	133147	2.88	0.72
4	Peak4	14.743	3051	0.07	0.76
5	Peak5	15.579	20209	0.44	0.80
6	Peak6	16.180	1204	0.03	0.83
7	Peak7	18.323	2461	0.05	0.94
8	Peak8	18.533	2347	0.05	0.95
9	COMP-3	19.436	4174559	90.45	1.00
10	Peak10	19.619	113019	2.45	1.01
11	Peak11	20.832	3999	0.09	1.07
12	Peak12	21.157	5984	0.13	1.09
13	Peak13	21.287	23452	0.51	1.10
14	Peak14	23.520	6456	0.14	1.21
15	Peak15	23.712	102766	2.23	1.22
16	Peak16	24.699	4995	0.11	1.27

Reported by User: Partha Pratim Bal (PB0112721)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 72940
 Page: 2 of 2

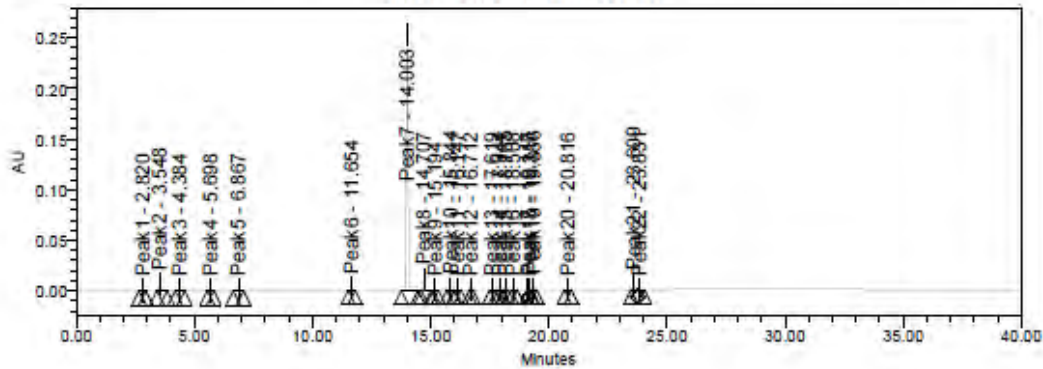
Project Name: QCHPLC041
 Date Printed:
 04-06-2021
 07:57:59 Asia/Kolkata

Attachment-50-HPLC

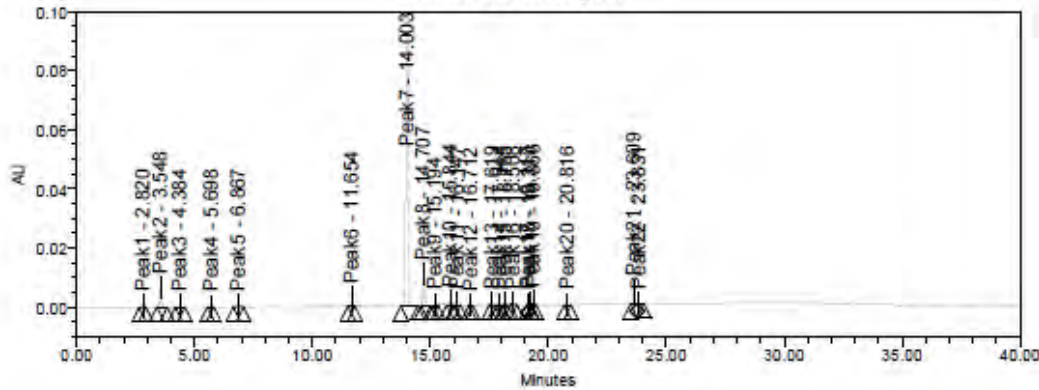
TCGLS_Report_ZOOM

SAMPLE INFORMATION			
Sample Name:	CRSD-19036-84-CR2	Acquired By:	SP0113317
Sample Type:	Unknown	Sample Set Name:	TCGLS_300621
Vial:	73	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 260.0 nm (2998)
Date Acquired:	01-07-2021 03:15:17 IST	Column Name:	XTERRA RP18(250X4.6)mm,5µ
Date Processed:	01-07-2021 08:12:31 IST		

Auto-Scaled Chromatogram



Zoom- Chromatogram



Reported by User: Sandip Shyam (SS0113466)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 72940
 Page: 1 of 2

Project Name: QCHPLC041
 Date Printed: 01-07-2021
 08:13:17 Asia/Kolkata

Peak Results

	Name	RT	Area	% Area	RT Ratio
1	Peak1	2.820	2241	0.16	0.20
2	Peak2	3.548	39458	2.61	0.25
3	Peak3	4.384	2596	0.18	0.31
4	Peak4	5.698	1931	0.14	0.41
5	Peak5	6.867	7772	0.55	0.49
6	Peak6	11.654	12395	0.88	0.83
7	Peak7	14.003	1231651	87.64	1.00
8	Peak8	14.707	50786	3.61	1.05
9	Peak9	15.194	2104	0.15	1.09
10	Peak10	15.844	6835	0.49	1.13
11	Peak11	16.147	2763	0.20	1.15
12	Peak12	16.712	412	0.03	1.19
13	Peak13	17.619	1762	0.13	1.26
14	Peak14	17.944	1161	0.08	1.28
15	Peak15	18.165	2822	0.20	1.30
16	Peak16	18.508	3437	0.24	1.32
17	Peak17	19.117	356	0.03	1.37
18	Peak18	19.210	1434	0.10	1.37
19	Peak19	19.366	5539	0.39	1.38
20	Peak20	20.816	937	0.07	1.49
21	Peak21	23.609	25183	1.79	1.69
22	Peak22	23.831	1838	0.13	1.70

Reported by User: Sandip Shyam (SS0113488)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 72940
 Page: 2 of 2

Project Name: QCHPLC041
 Date Printed:
 01-07-2021
 08:13:17 Asia/Kolkata

Attachment-51-1HNMR

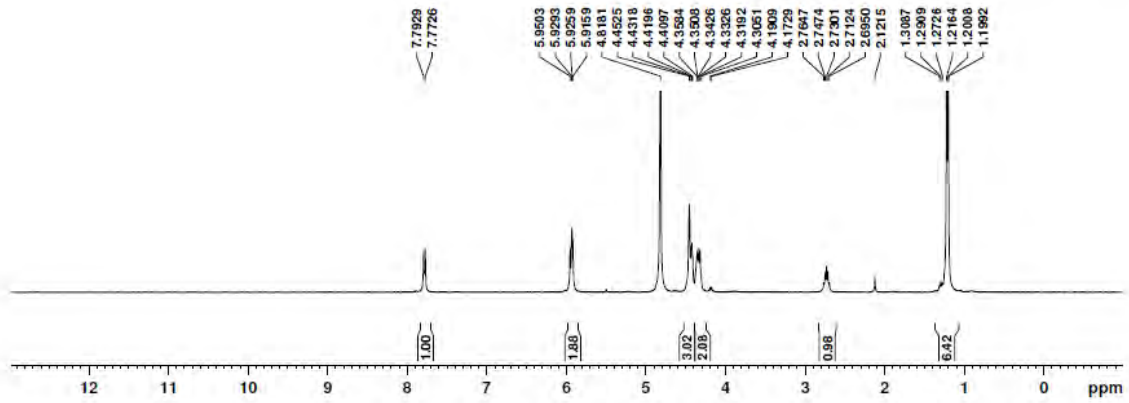
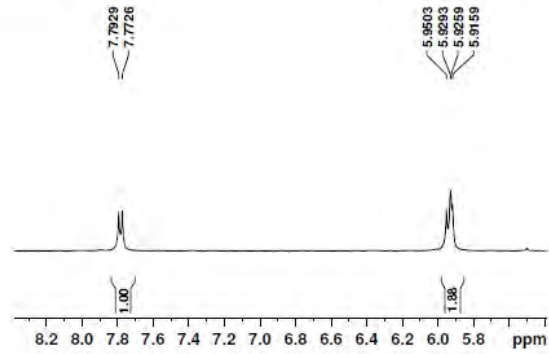
TCG Lifesciences Private Limited
Kolkata

CR592-16036-37-F3 IN D2O

TCGLS/ARD/NMR01/K01

```

NAME CR592-16036-37-F3
EXPNO 1
PROCNO 1
Date_ 20210420
Time 14:42:51
INSTRUM spect
PROBHD ZBG4B_504B 5PH
PULPROG zgpg30
TD 24096
SOLVENT D2O
NS 8
DS 8
SWH 8013.000 Hz
FIDRES 0.166776 Hz
AQ 1.4925964 sec
RG 320
DE 62.00 mmHg
TE 300.2 K
D1 1.00000000 sec
TD 400.1224000 MHz
SFO1 400.1224000 MHz
NUC1 1H
P1 6.00 usec
PL 0.00 dB
SI 16384
SF 400.0999200 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
    
```

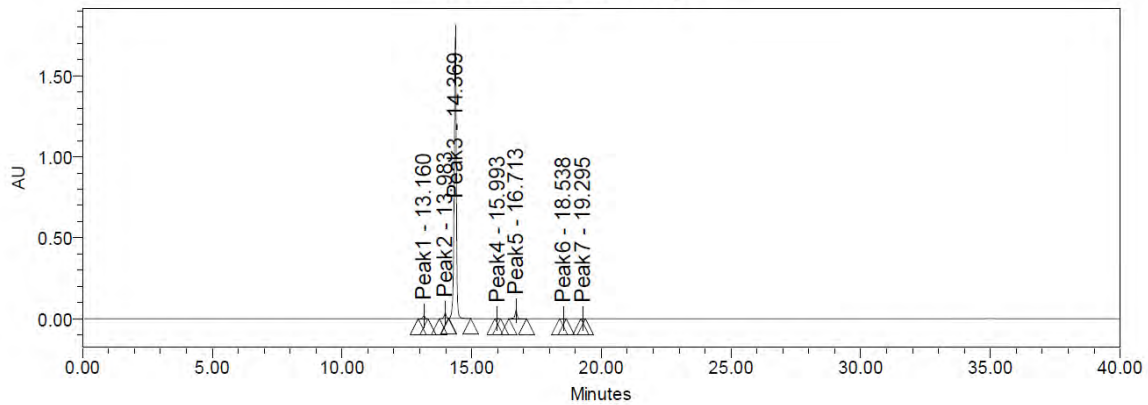


Attachment-52-HPLC

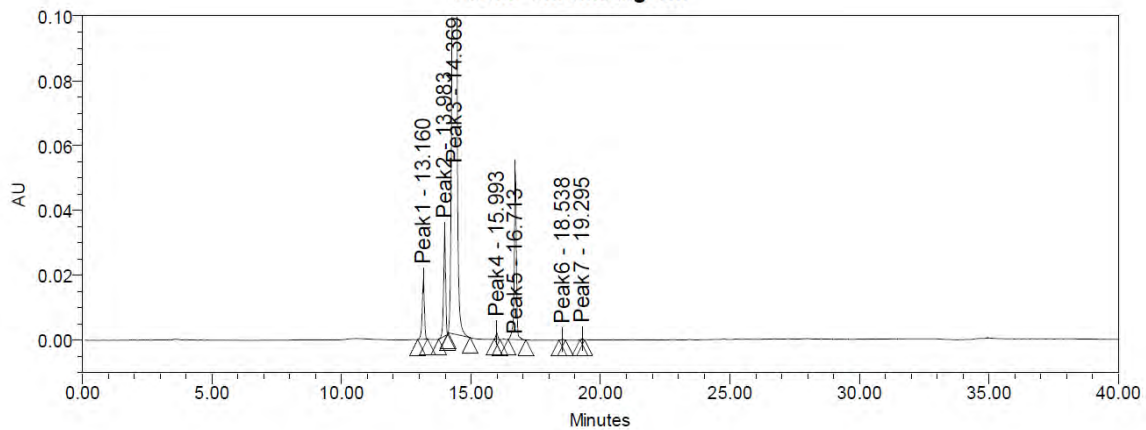
TCGLS_Report_ZOOM

SAMPLE INFORMATION			
Sample Name:	CR592-16036-37-F3	Acquired By:	SP0113317
Sample Type:	Unknown	Sample Set Name:	TCGLS_200421A
Vial:	30	Acq. Method Set:	EIDD_CP_METH
Injection #:	1	Processing Method:	EIDD
Injection Volume:	10.00 ul	Channel Name:	260.0nm
Run Time:	40.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 260.0 nm (2998)
Date Acquired:	20-04-2021 14:42:12 IST	Column Name:	XTERRA RP18(250X4.6)mm,5µ
Date Processed:	20-04-2021 15:27:49 IST		

Auto-Scaled Chromatogram



Zoom- Chromatogram



Reported by User: Asif Mondal (AM0113345)
 Report Method: TCGLS_Report_ZOOM
 Report Method ID: 55455
 Page: 1 of 2

Project Name: QCHPLC041
 Date Printed: 20-04-2021
 15:28:43 Asia/Kolkata

Peak Results

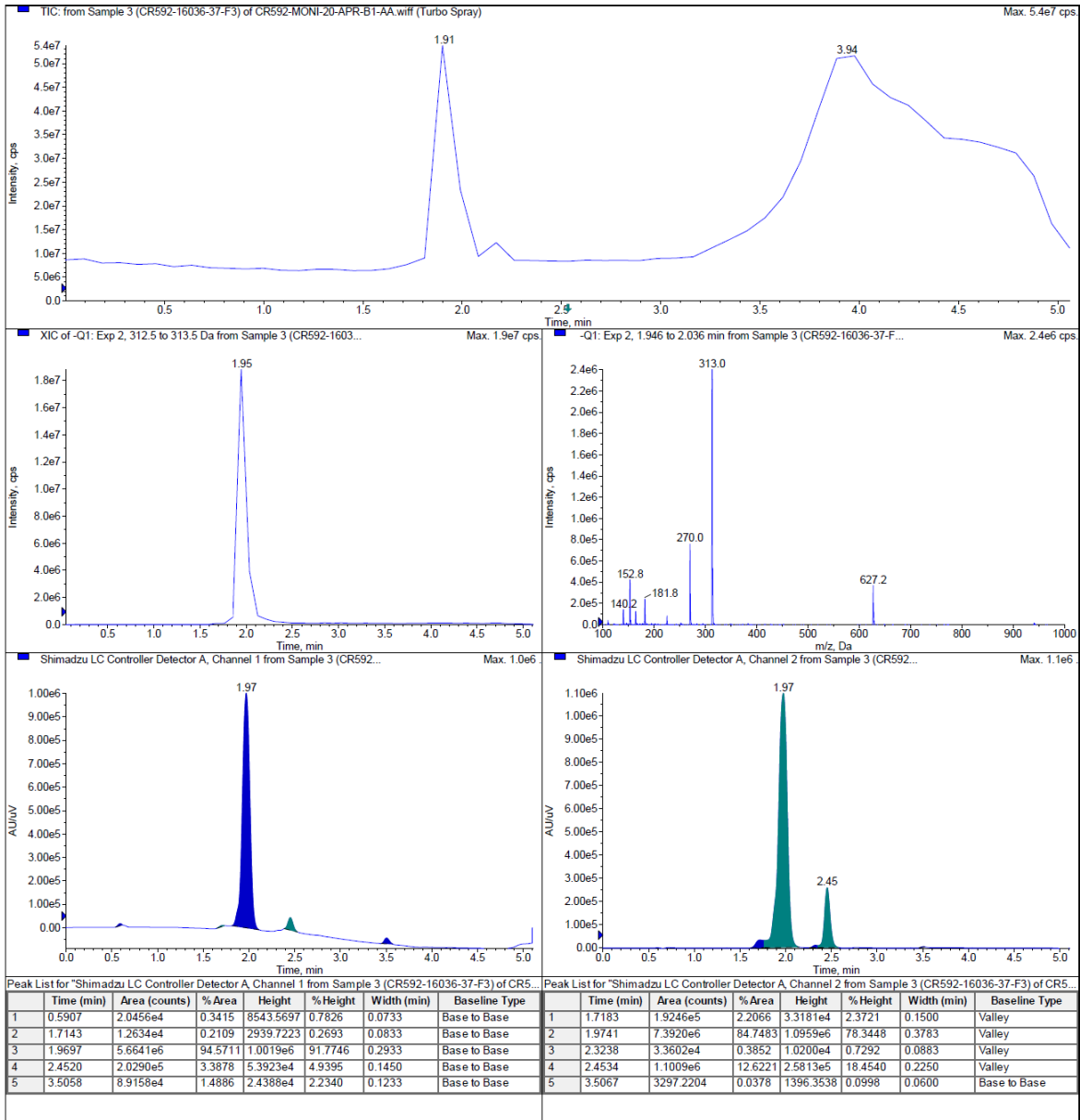
	Name	RT	Area	% Area	RT Ratio
1	Peak1	13.160	107974	1.04	0.92
2	Peak2	13.983	173160	1.66	0.97
3	Peak3	14.369	9839808	94.33	1.00
4	Peak4	15.993	10349	0.10	1.11
5	Peak5	16.713	296919	2.85	1.16
6	Peak6	18.538	1662	0.02	1.29
7	Peak7	19.295	1787	0.02	1.34

Attachment-53-LCMS

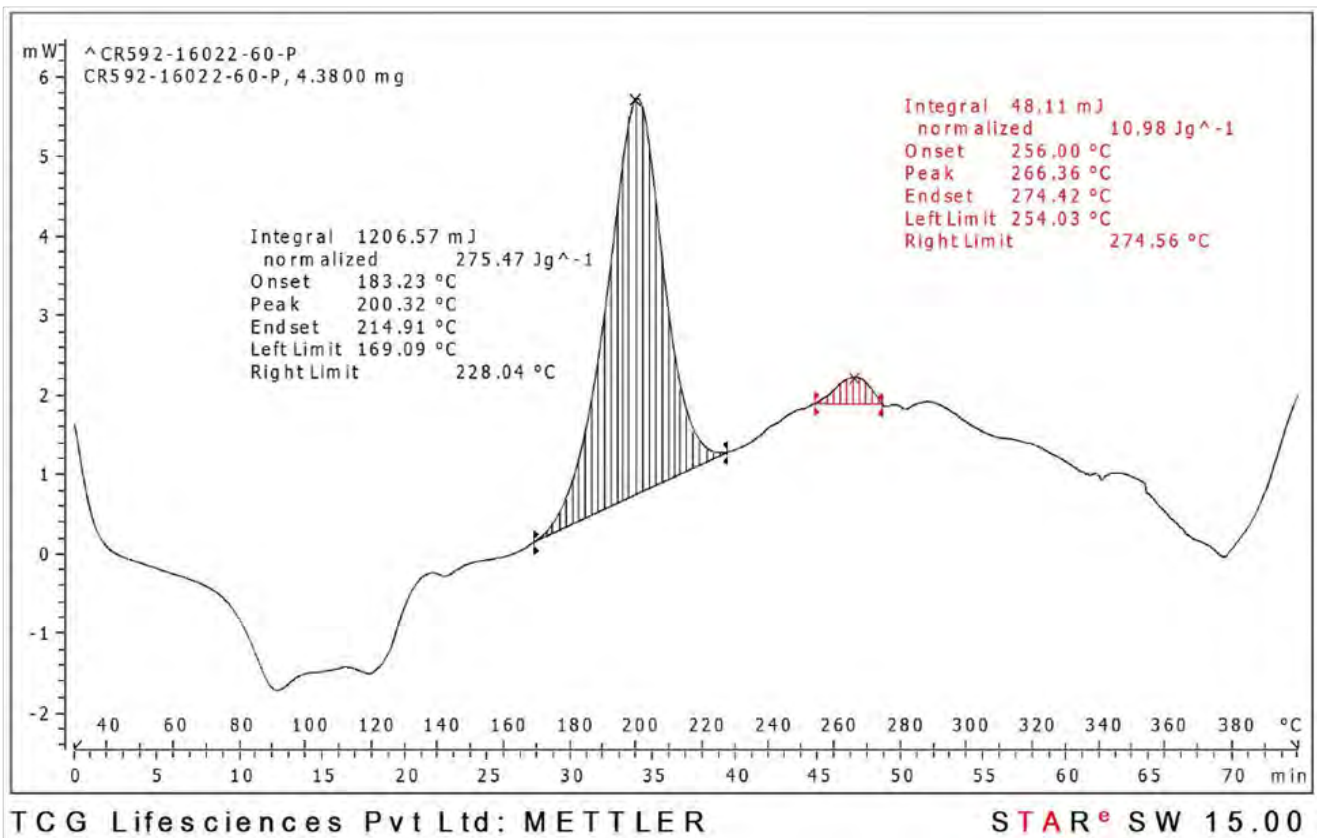
Sample Name: CR592-16036-37-F3

Acq. Time: 15:14

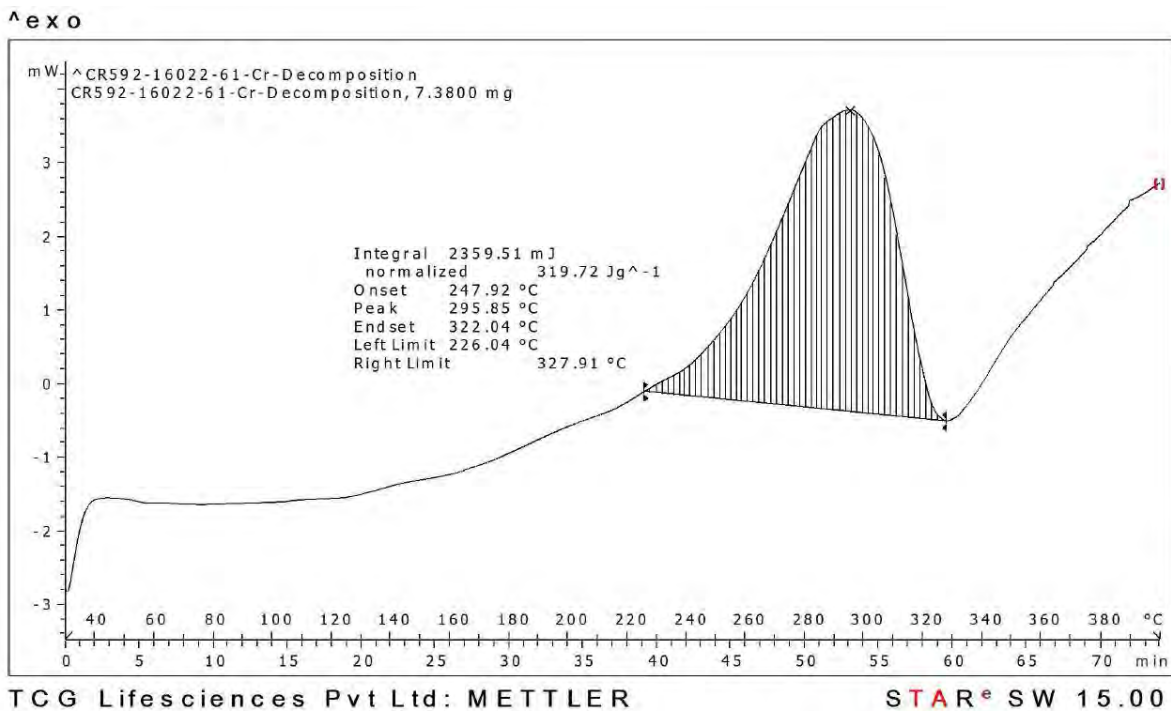
Acq. Date: Tuesday, April 20, 2021



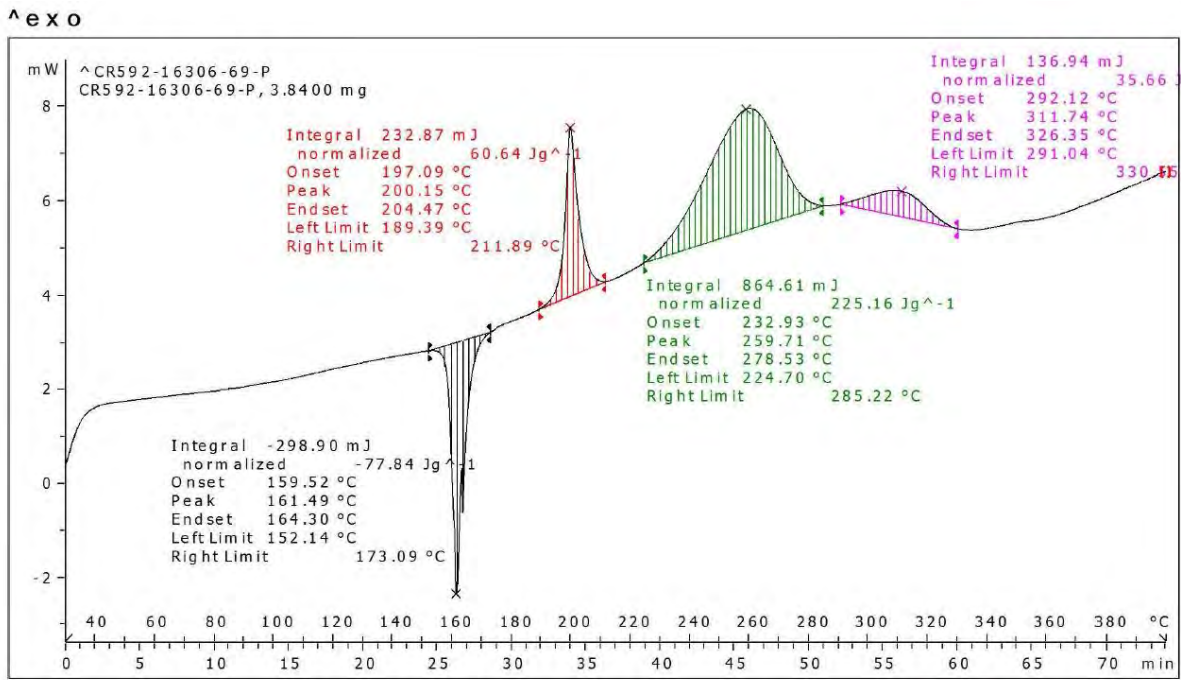
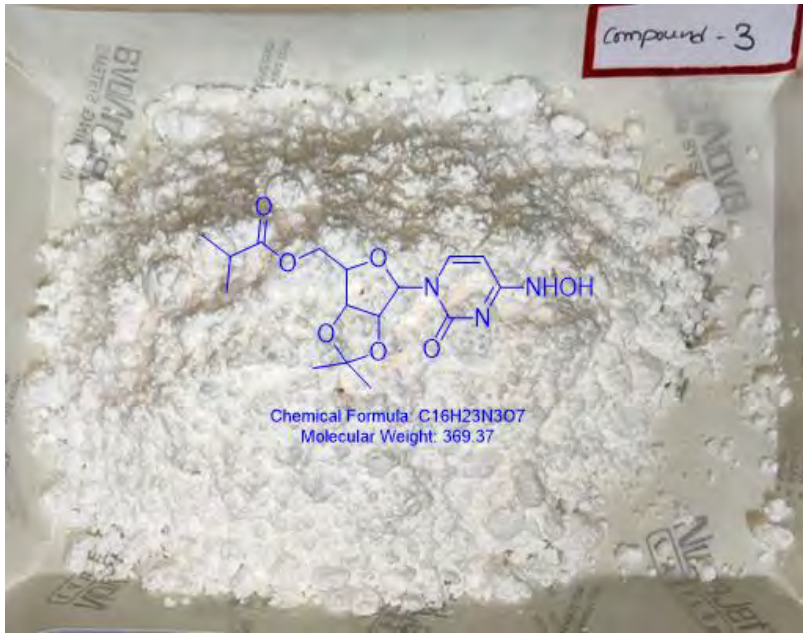
Attachment-54-DSC



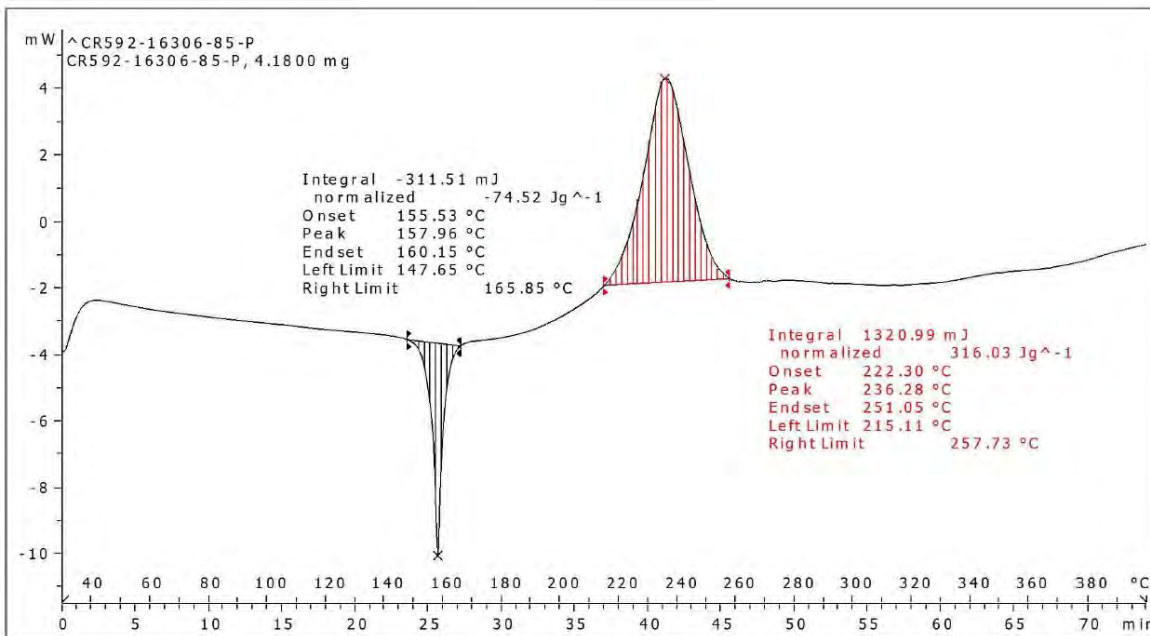
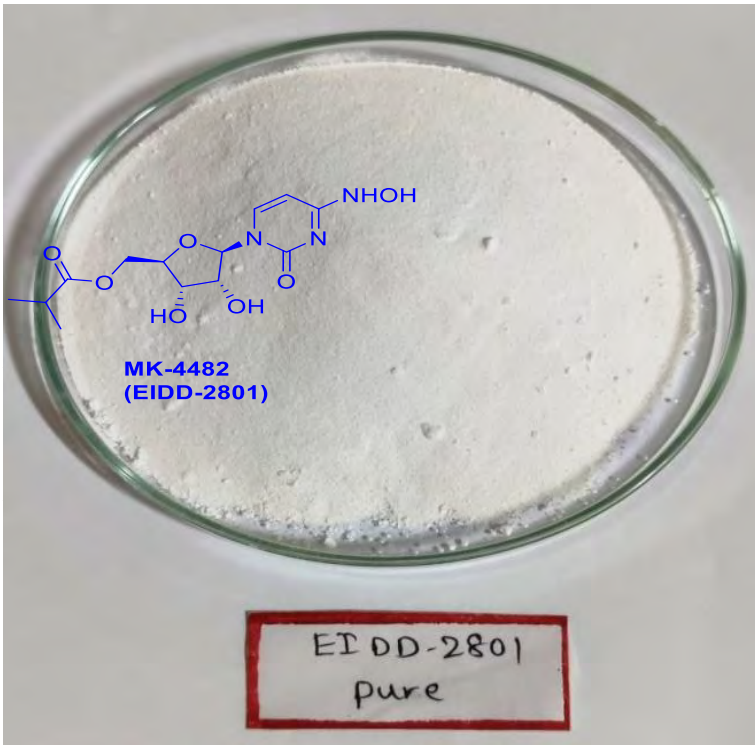
Attachment-55-DSC



Attachment-56-DSC



Attachment-57-DSC

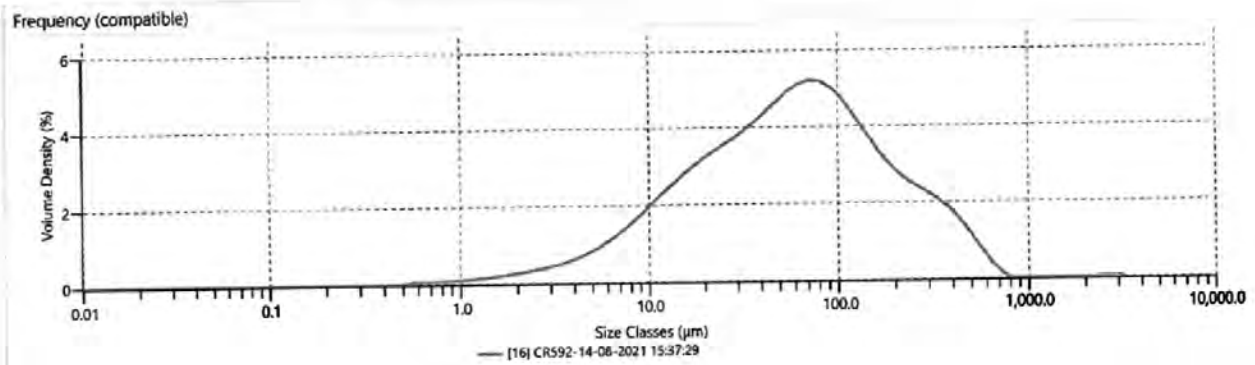


Attachment-58-PSD data

Analysis Dry Report



Measurement Details Operator Name RLPL075 Sample Name CR592 SOP File Name EIDD(DRY)TCG LIFE_SOP.msop Batch No: CR592-16492-32-P	Measurement Details Analysis Date Time 14-08-2021 15:37:29 Measurement Date Time 14-08-2021 15:37:29 Result Source Measurement
Analysis Particle Refractive Index 1.590 Particle Absorption Index 0.100 Dispersant Name Dry dispersion Dispersant Refractive Index 1.000 Scattering Model Mie Analysis Model General Purpose Weighted Residual 0.41 % Laser Obscuration 3.56 % Concentration 0.0085 %	Result Uniformity 1.283 Specific Surface Area 277.8 m ² /kg D [4,3] 98.9 μm Dv (10) 9.87 μm Dv (50) 57.4 μm Dv (90) 255 μm Air Pressure Demand 2.0 barg Feed Rate Demand 45



Size (μm)	% Volume Under	Size (μm)	% Volume Under	Size (μm)	% Volume Under	Size (μm)	% Volume Under	Size (μm)	% Volume Under	Size (μm)	% Volume Under	Size (μm)	% Volume Under	Size (μm)	% Volume Under
0.0100	0.00	0.0463	0.00	0.214	0.00	0.991	0.35	4.58	1.08	21.2	23.36	88.1	67.98	434	97.85
0.0114	0.00	0.0128	0.00	0.243	0.00	1.13	0.45	5.21	4.35	24.1	26.20	111	71.93	516	98.71
0.0129	0.00	0.0291	0.00	0.276	0.00	1.28	0.57	5.83	5.14	27.4	29.18	127	75.57	586	99.43
0.0147	0.00	0.0679	0.00	0.314	0.00	1.45	0.71	6.72	6.08	31.1	32.31	144	78.86	666	99.84
0.0167	0.00	0.0771	0.00	0.357	0.00	1.65	0.87	7.64	7.19	33.4	35.60	163	81.30	754	100.00
0.0189	0.00	0.0875	0.00	0.405	0.00	1.88	1.07	8.68	8.49	40.1	39.09	186	84.44	859	100.00
0.0215	0.00	0.0995	0.00	0.460	0.00	2.13	1.29	9.86	9.99	45.6	42.78	211	86.84	976	100.00
0.0244	0.00	0.113	0.00	0.523	0.00	2.42	1.56	11.2	11.71	51.8	46.69	240	89.00	1113	100.00
0.0276	0.00	0.128	0.00	0.594	0.06	2.75	1.87	12.7	13.64	58.9	50.81	272	91.07	1280	100.00
0.0315	0.00	0.146	0.00	0.675	0.12	3.12	2.22	14.5	15.79	66.9	55.09	310	92.97	1430	100.00
0.0358	0.00	0.164	0.00	0.787	0.19	3.55	2.63	16.4	18.14	76.0	59.45	352	94.73	1630	100.00
0.0407	0.00	0.188	0.00	0.927	0.27	4.03	3.11	18.7	20.67	86.4	63.79	400	96.31	1850	100.00

Text Box

Analysed By: *[Signature]*
 Date: 14/08/2021

Text Box

Checked By: *[Signature]*
 Date: 14/08/2021

Attachment-59-PXRD data

