ChemGenes CORPORATION

established in 1981

Manufacturer of the
widest variety & **highest quality**
Phosphoramidites & Solid Supports
for the biopharmaceutical, diagnostic, &
academic markets

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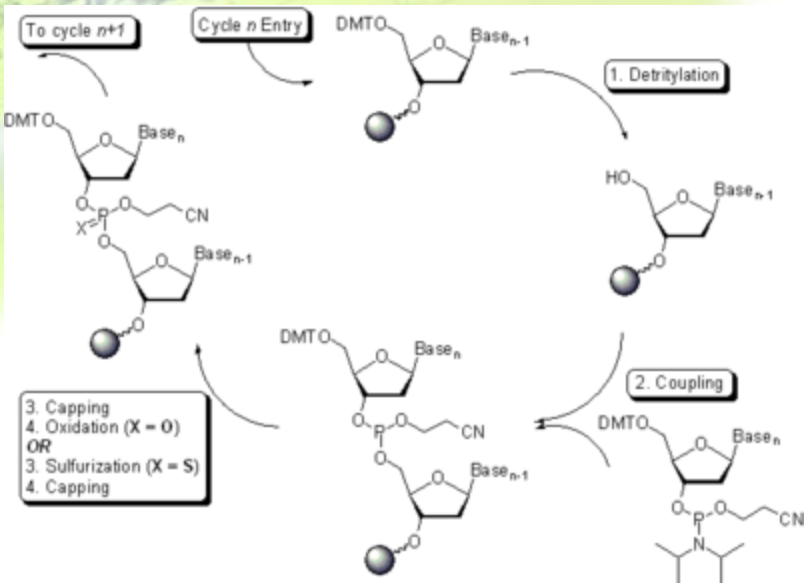
Our Manufacturing Processes

- Chemical Synthesis of Nucleic Acid Compounds and are required to be very High Quality



- Processes include Organic Reactions (Phosphitylation), Solid Support Derivatization & Purification Techniques

- Purification Processes include Extraction, Crystallization, Precipitation, Column Chromatography

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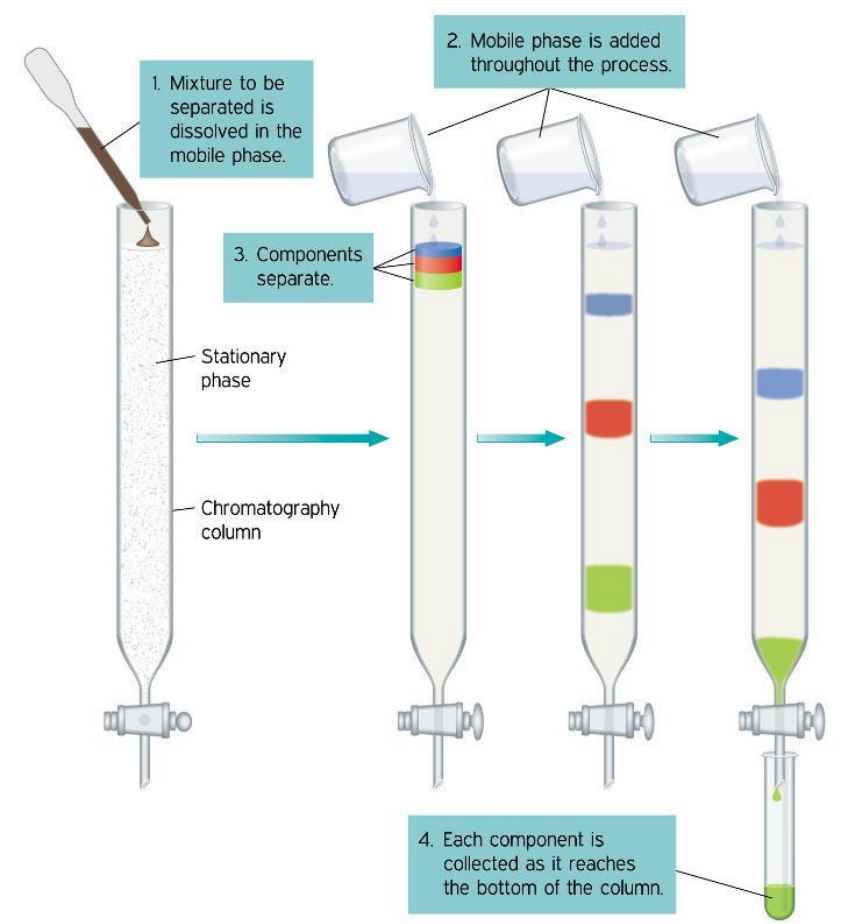
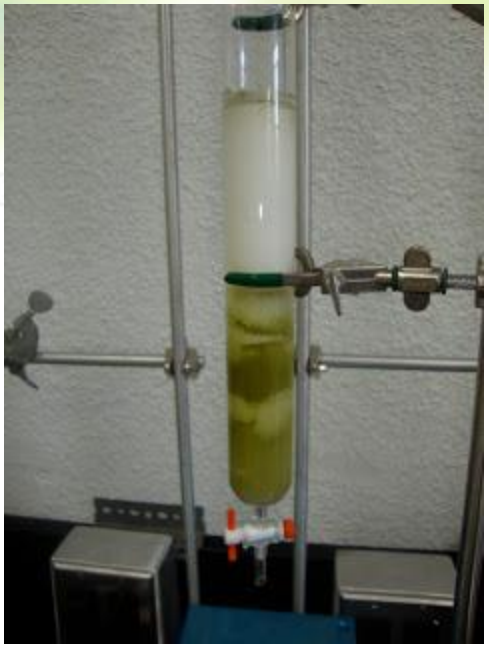
Column Chromatography





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Our Responsibility

- Business and Institutions have a fiduciary responsibility to the environment and workplace safety
- Most business owners want to be in compliance but often are not aware or do not understand the regulations
- Government Resources (OTA) and Private Consultants guide us!

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Our History of TUR - 2008

- First TUR Plan filed in July 2008, prepared by Goldman Environmental
- Scope covered Acetone, Chloroform, Ethyl Acetate, and Hexane. Other solvents below reportable quantity threshold
- Focus on Column Chromatography:
  Design on Experiments… reformulation to improve production efficiency (report mentions possibility of recycling)
- An average 1kg batch of final product used approximately 22kg of silica gel and 160L of solvent!
- Some “Bulk” products required multiple chromatography steps…

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Our History of TUR - 2010

- 2010 TUR Plan focused on Pressure Chromatography for Bulk Production

- Scope covered:
  - Chloroform,
  - Ethyl Acetate, and
  - Hexane
  - (Acetone below threshold)

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Solvent Reductions

	2007	2008	2009	2010	2011	2012
Chloroform	82706	75698	40374	37106	36948	23946
Ethyl Acetate	48726	48017	43810	36840	39936	37256
Hexane	26517	25507	15846	17114	22120	17108
pro. Ratios	NA	1.15	0.85	0.9	1	1

2012 TUR Plan focuses on Solvent Recycling for Bulk Production

→ reduction of substituted Ethyl Acetate and Hexane

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Challenges Solvent Recycling

- Justification of Cost Benefit (Labor, Energy, Yield Loss)
- Quality of Recovered Solvent including Cross Contamination possibility
- Cost of Analytical Component
- Qualification Process and Time

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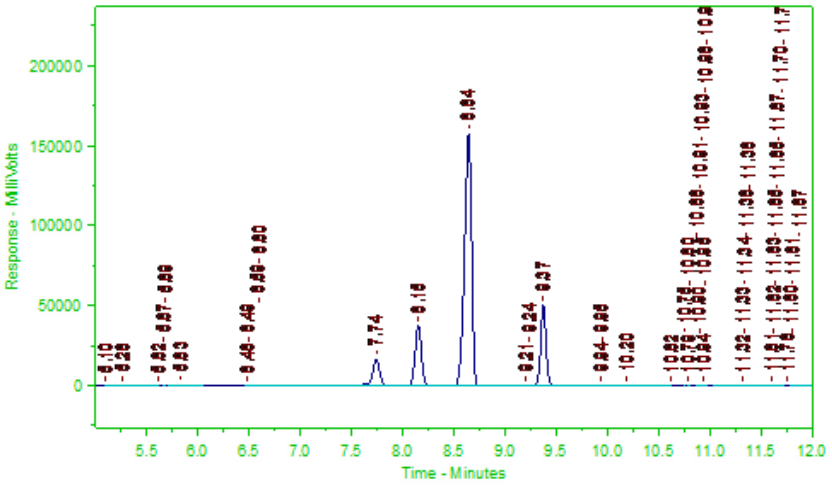
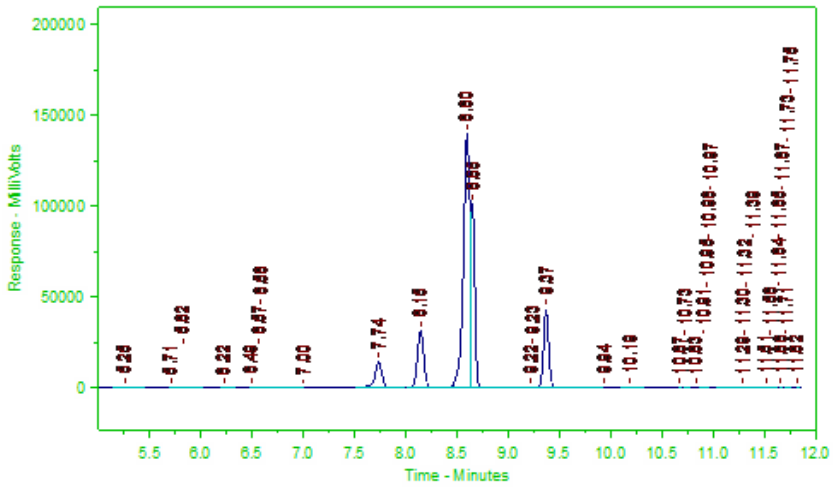
Qualification Process

Hexane(s) GC Result



Hexane(s) + Ethyl Acetate GC Result



RT = 7.7min, Hexane Isomer (2-MethylPentane)

RT = 8.2min, Hexane Isomer (4-MethylPentane)

RT = 8.6min, n-Hexane

RT = 9.4min, Hexane Isomer (MethylCyclopentane)

RT = 8.8min, Ethyl Acetate (appears as merged peak with n-Hexane)

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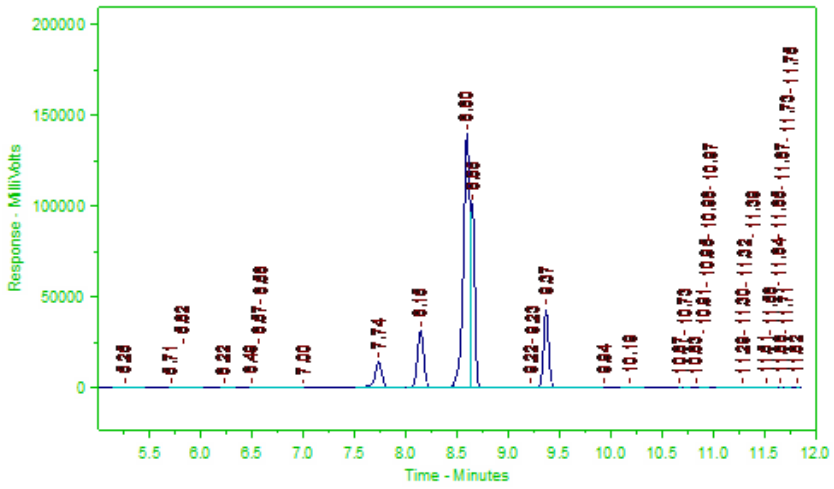
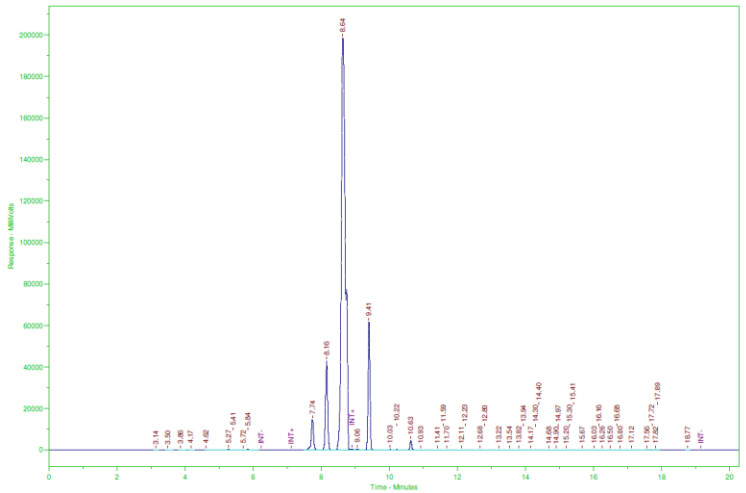
Qualification Process

Hexane(s) + Ethyl Acetate GC Result



Recycled Solvent System



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Fractional Distillation

- Instrument Purchased from CBG Technologies
- TechnoClean F-2500, Fractional Distillation System
- Recommended by Gus at OTA

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Fractional Distillation, specs

- 25gal capacity (94.5L)
- Air Cooled – no water hookup
- Redundant Safety features and auto shut down
- Auto Fill Pump – no need to pour
- HDPE Bag for easy waste removal
- claim >99.9% purity of recovered solvent
- Custom Programming for multiple solvents and solvent systems

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Fractional Distillation, results

- Ethyl Acetate and Hexane(s)
- Average batch size ~45L
- Maximum Batch Size = 75L
- Average recovery of >90-95%

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results, continued

- Re-Used in DNA Cytidine (dC-Ac CEP) compound and 2 batches of a Modified DNA compound (2’-F-dU CEP)

- Batch Size of each was 1kg each

- Both Batches passed and met the same rigid specifications for release!

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Cost Benefit

process A	ratio	cost / L	extended
Ethyl Acetate	30	$ 3.00	$ 0.90
Hexane	70	$ 2.00	$ 1.40
			$ 2.30

process B	ratio	cost / L	extended
Ethyl Acetate	80	$ 3.00	$ 2.40
Hexane	20	$ 2.00	$ 0.40
			$ 2.80

Savings per Cycle

	Usage (L)	recovery %	recover (L)	RM savings	Waste Savings
rxn	10	0			
A	120	92	110.4	$ 253.92	$ 55.20
B	90	92	82.8	$ 231.84	$ 41.40
				$ 485.76	$ 96.60
			Savings for Total Cycle:		**$ 582.36**

Additional Costs

cost of equipment	$ 25,500.00	one time	cost of S3000
utilities	$ 3.20	per day	3.20 per batch per CBG
Labor (1hr/day - load, empty, clean)	$ 32.00	per day	
inner liner bags	$ 4.00	per bag	2 uses per change, PP30N $200/25 units
Drying Station (dessicant, alumina)	$ -	$/L	500L/change - $350/unit
cost of GC or GC/MS analysis	$ 45.00	per sample	
Total Cost per Cycle:	**$ 84.20**		

bulk products on MPLC:	17	
est. cycles per product after 1st run	4	
	68	total cycles
	$ 498.16	net savings
	$ 33,874.88	

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Savings

Parameters

Solvent X	$3.20/L
Solvent Y	$2.15/L
Labor rate – 1 hour at $30/hr	$30.00/batch
Inner liner bags – 10 uses/change	$0.80/batch
Quality Control – GC-MS	$45.00/sample
Maintenance $1000/yr & 200runs/2yr	$7.95/batch
Electricity Consumption	$0.80/batch
Waste Disposal: 75 liners/25gal pail	$5.00/batch

Hazardous waste cost (including transportation, disposal, regulatory fees, insurance costs)	$149.50/200L

Usage and Costs for Four Months	Quantity/Costs
Input solvent	1339 L
Output solvent	1308 L
% recovery	97.70%
Material and Waste Savings	
With 97.70% return, Solvent savings	$3,475.76
Hazardous Waste Savings	$1,000.90
Total Material and Waste Savings:	**$4,476.67**
Labor and QC Costs	
Labor	$810.00
QC	$1215.00
Total Labor and QC Costs:	**($2,025.00)**
Operation and Maintenance Costs	
Maintenance	$214.65
Tank Liners	$21.60
Electricity	$107.20
Waste Disposal	$135.00
Total O&M Costs:	**($478.45)**
Total Savings:	**$1,973.22** Over 27 batches or $73.27 per batch

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Special Thanks to:

Toxic Use Reduction Institute-UMASS Lowell

Office of Technical Assistance

Goldman Environmental

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