

Product Update:

Low Water - Amine Free Biotech Solvents Acetonitrile DMF NMP

I. Introduction:

High Purity Solvents are required for optimal performance in peptide as well as RNA/DNA synthesis (Oligonucleotide synthesis). Air and water contamination impede the reaction and have the added effect of degrading these solvents creating free amines which have a significant adverse effect on the synthesis inhibiting both rate and yield.

Utilizing solvents of high purity is essential. Maintaining low water and free-amine contamination is optimal. Traditional methods of preparation to achieve these purity levels would combine the purification of the solvent with a system of packaging to minimize environmental exposure and product degradation. Products that are commercially available today include purification and packaging in pressurized cylinders or containers with septums. Both of these methods maintain an adequate level of product integrity but they are costly or inconvenient. In addition neither of these methods continues to remove contaminants through the use of the product that forms from user contamination or the breakdown of the product due to exposure to air and moisture.

Only Pharmco Products has addressed all these issues with an extremely cost efficient technology route that achieves purity levels equal and superior to the best brands on the market, while maintaining the purity level through the full use of the product.

Molecular Traps Inside The Bottle

Pharmco's Biotech Solvents utilize Molecular Trap Technology.

These molecular traps are placed inside the 4-liter bottle and remain there through the use of the solvents. The molecular trap remains active through the life of the solvent continually removing moisture and free amines from the solvent. Due to this, the user can consume the entire contents of the 4-liter bottle without worry of contamination and product degradation through the multiple openings of the container. The Molecular Trap itself is a patented inert solid enclosed in a sub-micron mesh which allows for the flow of contaminants into the trap but does not allow for any back contamination into the solvent.

Convenient 4 liter Glass Bottles

Since 4 liter bottles can be utilized, customers can purchase as little as one case (4x4 liters) rather than a pressurized cylinder. They can easily dispense any desired quantity rather than dealing with needles and septum. They can also save a lot of money due to the economics of the standard 4x4 liter case quantity and the cost efficiencies of the Molecular Trap. Users do not have to worry about wasted product. The Molecular Trap remains active and continues to purify the solvent through the full use of the 4-liter bottle. Not a single drop is wasted!

II. Detail on the Biotech Solvents:

a.) Acetonitrile (ACN):

Low water Acetonitrile is essential for the synthesis of oligonucleotides. Automated DNA synthesizers typically utilize a large ACN reservoir for column washing during synthesis. The bottle may stay on an instrument for a week or more and will continually pick up moisture even if protected by an inert atmosphere due to the extremely hygroscopic nature of ACN.

This can be particularly troublesome during the humid summer months especially if the bottle also serves as the amidite diluent. Maintaining moisture levels below 50 ppm is crucial and below 20 ppm is optimal.

Pharmco Biotech Grade of Acetonitrile with Patented Molecular Traps achieves these levels through the full use of the product as it continues to absorb moisture from ACN through to the last drop!

After extensive development, Pharmco Biotech Grade of Acetonitrile was field tested at several leading Universities. The result was that Pharmco Biotech Acetonitrile provides an extremely cost efficient and flexible alternative to similar high purity, low water products from other leading vendors.

"Total oligo yields are as good or better than low water Acetonitrile from other vendors. We will be placing another order soon..."

Note: Testing moisture levels by Karl Fisher or similar methods in Acetonitrile can be very tricky. Acetonitrile absorbs moisture so quickly that a sample of Acetonitrile with less than 10 ppm water will test much higher unless special techniques and equipment are used. Pharmco's Biotech Acetonitrile with Molecular Traps maintains moisture level at less than 10 ppm. Normal testing by Karl Fisher will yield 20-30 ppm utilizing conventional Karl Fisher techniques and equipment.

b.) Dimethylformamide (DMF):

DMF is a primary solvent for peptide synthesis. Water and free-amines are primary contaminants. The free-amine, Dimethylamine (DMA) is present as a normal contaminant during production of DMF and as a breakdown product of DMF. Moisture serves to hydrolyze DMF to create even higher levels of DMA.

DMF like Acetonitrile is hygroscopic and will continue to absorb water and therefore continue to form DMA as the solvent ages.

The level of free amines (DMA) is crucial to peptide yield. Dimethylamine (DMA) is the primary free-amine contaminant in DMF. DMF is an unstable product that continually breaks down forming DMA as a contaminant even under the best storage and packaging conditions. **As a result Molecular Trap technology is uniquely and ideally suited to this problem as it continually removes free amines from the solvent as they are formed as well as moisture which leads to DMF degradation to DMA.**

Pharmco's Biotech Grade of DMF utilizing Molecular Traps brings the moisture level well below 100 ppm while maintaining free amine levels to below 1 ppm!

Pharmco's Biotech Grade of DMF was field tested at several leading Universities. The results were outstanding in regard to total yield as well as cost savings over similar high purity products from leading vendors.

Sigma-Genosis, one of the largest manufacturers of peptide sequences in the USA switched to Pharmco's Biotech Grade of DMF citing both ease of use over pressurized cylinders as well as cost efficiencies. Reaction yields have been equal to or superior to the previous product. Researchers do not have to dispense DMF into portable containers and then worry about utilizing the solvent in a short period of time.

c.) 1-Methyl-2-Pyrrolidone (NMP):

NMP is also used in biotech applications and synthesis. Moisture and free amine contamination are both poisons inhibiting both rate and yield. The main amine contaminant is Methylamine. Methylamine is present as a by-product of NMP production. Pharmco Biotech Grade of NMP maintains water levels well below 100 ppm and Methylamine levels below 10 ppm. Pharmco Biotech Grade of NMP has been field tested and approved by several leading Universities and leading independent commercial companies.

III. Patented Molecular Traps:

a.) Application:

Molecular Traps are an exciting application of existing technology to the problems associated with solvent purification. Molecular Trap cartridges are manufactured and wrapped in evacuated foil packets. Once the target solvent is purified and packaged the Molecular Trap is placed directly in the 4-liter bottle. From the initial second the Trap touches the solvent to the last drop used in the bottle, the Molecular Trap remains active, continually purifying the solvent. Research has shown that 7-14 days is necessary to assure the maximum benefit of the Molecular Trap in the solvents. Pharmco Biotech Solvents are all dated. Not with the typical expiration date but with a "Do not use before" date.

Ironically, due to the active nature of the Molecular Trap, the solvent actually gets "better with age".

b.) Quality Control/Quality Assurance:

Each manufactured lot of Molecular Traps is use-tested by quantifying amine removal from commercial sources of solvent.

c.) Materials:

Molecular Traps are designed and manufactured to withstand long-term in-situ, solvent exposure while maintaining full filtration of particulates. Molecular Traps are made from an inert microporous, electronics grade, membrane material. The effective filtration of the membrane is 0.2 microns. This membrane material is tested safe for long term exposure to the solvents it is used to actively purify.

d.) Disposal:

Molecular Traps are non-hazardous. Once the solvent in the 4-liter bottle has been used, the trap, with the bottle can be disposed in accordance with the normal procedures of your company or institution as well as Local, State and Federal Law.

Specifications:

Acetonitrile- Biotech Grade- Low Water/Amine Free

Gas Chromatographic Analysis of this product using an electron capture detector shows no peaks with a response greater than 5 pg/ml as Heptachlor Epoxide

Product	Grade Certifications	CH3CN	CAS 75-05-8	FW 41.05	1L=0.78 kg
Catalog # AC0018-G	Package Sizes	Product Specifications	Limits	Typical	
3000ANHIOCS4L	4 x 4 liter glass bottles	Water, wt% max.	10 ppm	<5 ppm	
		Free Amines	<1 ppm	<1 ppb	
		GC-ECD	10 ppt max	1.0 ppt	
		UV Absorbance @	A.U	A.U	
		190 nm	1.000 max	0.3540	
		195 nm	0.150 max	0.0650	
6.87 lbs. net / 4 liter		200 nm	0.070 max	0.0100	
		205 nm	0.050 max	0.0050	
		210 nm	0.040 max	0.0040	
		220 nm	0.020 max	0.0000	
		254 nm	0.010 max	0.0000	
		Assay, (GC), min	99.9%	99.98%	
		Residue After Evaporation	3 ppm max	<1 ppm	
		Fluorescence Background	1 ppb	<1 ppb	
		Color (APHA), max	10	3	
		Appearance	Clear	Clear	
		Titration Acid, max.	0.001 meq/g	0.0007	
		Titration Base, max	0.0001 meq/g	<0.0001	
		Substances Red. KMnO4	To Pass Test	Pass	
		Identification (IR/GC)	To Conform	Pass	
		Filtered to 0.2 microns max.	Per Lot	Pass	

n,n-Dimethylformamide (DMF) - BIOTECH - Low Water / Amine Free

Gas Chromatographic Analysis of this product using an electron capture detector shows this product suitable for the above applications.

Product Grade Certifications HCON(CH₃)₂ CAS 68-12-2 FW 73.09 1L=0.95 kg

Catalog #	Package Sizes	Product Specifications	Limits	Typical
324BIODISCS4L	4 x 4 liter glass	GC-ECD	To Pass	Pass
7.91 lbs. net / 4 liter		Free Amines	1 ppm max	<1 ppb
		UV Absorbance @	A.U.	A.U.
		268 nm	1.000 max	0.653
		275 nm	0.300 max	0.147
		290 nm	0.100 max	0.046
		310 nm	0.050 max	0.013
		340 nm	0.010 max	0.001
		Assay, (GC), min	99.9%	99.99%
		Residue After Evaporation	5 ppm max	< 2 ppm
		Color (APHA), max	10	<10
		Appearance	Clear	Clear
		Titration Acid, max.	0.003 meq/g	Pass
		Titration Base, max	0.0005 meq/g	Pass
		Aldehyde (as HCHO), max	0.002%	Pass
		Water, max	0.01%	<0.01%
		Specific Gravity @ 15.5C	0.953-0.955	Pass
		Identification (IR/GC)	To Conform	Pass
		Filtered to 0.2 microns max	Per Lot	Pass

Product	Grade Certifications	HOCH2CH2C4H7NCH3	CAS 872-50-4	FW 99.13
Catalog #	Package Sizes	Product Specifications	Limits	Typical
2525300 BIOCS4L	4 x 4 liter Glass	Assay, min.	99.0%	99.97%
		Color (APHA)	50 max	10
		Water	0.01% max	<0.01%
		Free amines (as CH3NH2)	10 ppm	<1ppb
		Chloride (Cl)	1 ppm	ND
		UV Absorbance @	AU	AU
		275 nm	1.00	Pass
		285 nm	0.15	Pass
		300 nm	0.05	Pass
		350 nm	0.01	Pass
		400 nm	0.01	Pass

Above Products are Purified, dried and distilled in glass and treated with an Amine Absorbing agent. Suitable for:
 All Biotech Applications including peptide synthesis and RNA-DNA work. This product contains a proprietary Water-Amine-Absorbing Agent enclosed in a submicron mesh which will continuously remove free amines and water during normal use of the solvent and with multiple openings of the container. The Absorbing Agent is solid matter and does not cause contamination.

Order from:

Clarkson Laboratory & Supply Inc

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 Fax: 619-425-7917
 www.clarksonlab.com

Pricing:

Catalog#	Description	Price
AC0018-G	ACETONITRILE (ACN) BIOTECH GRADE 4L	\$82.50 4ea/cs Less 25%
DC0063-G	N,N-DIMETHYLFORMAMIDE (DMF) BIOTECH 4L	\$57.00 4ea/cs Less 25%
MC0158-G	N-METHYL 2-PYRROLIDONE (NMP) BIOTECH GRADE 4L	\$82.50 4ea/cs Less 25%

Prices effective 01/01/02