ChemGenes CORPORATION

Exceptional Quality Products for Drugs and Diagnostics

- **Natural 2′-O-TBDMS-RNA Phosphoramidites**
  - · Standard: 2′-TBDMS-A^{Bz}, 2′-TBDMS-C^{Ac}, 2′-TBDMS-G^{iBu}, 2′-TBDMS-U.
  - · Mild (N-Acetyl protection): 2′-TBDMS-A^{Acetyl}, C^{Acetyl}, G^{Acetyl}.
  - · Ultra-Mild (N-Pac protection): 2′-TBDMS-A^{pac}, 2′-TBDMS-C^{pac}, 2′-TBDMS-G^{pac}.
- **2′-O-Methyl-RNA Phosphoramidites**
  - · 2′-O-methyl-A^{Bz}, 2′-O-methyl-C^{Ac}, 2′-O-methyl-G^{iBu} & 2′-O-methyl-G^{Ac}, 2′-O-methyl-U.
- **2′-O-Fluoro-RNA Phosphoramidites**
  - · 2′-O-fluoro-A^{Bz}, 2′-O-fluoro-C^{Ac}, 2′-O-fluoro-G^{iBu}, 2′-O-fluoro-U.
- **2′-O-Fluoro-RNA Phosphoramidites (Mild Deprotecting groups)**
  - · 2′-O-fluoro-C^{Ac}, 2′-O-fluoro-C^{Fmoc} [Patent Pending]
    2′-O-fluoro-GAc [Patent Pending]

Quality of our 2′- Fluoro phosphoramidites: HPLC > 98%; 31P NMR >99% consistently

Bulk Capabilities

multi-kilo batch sizes

UnyLinker Universal Support

As CPG and Polystyrene supports; Bulk supports and pre — packed columns
(Technology Licensed from Isis Pharmaceuticals for therapeutic and diagnostic applications)

Key Features:

- Fully compatible with standard phosphoramidite reagents and synthesis conditions
- Standard DMT group requiring standard deblock solutions for oligonucleotide synthesis
- Coupling efficiency ≥ 99%
- Results in 3′— OH oligonucleotides
- No detectable amount of 3′— phosphate
- Standard succinate linkage — cleavage from support is quantitative from aq. ammonia
- No base modification is observed
- Very minimum N-1 formation

Example of Oligo Synthesis:
A typical DNA sequence synthesis is illustrated:
Seq No.# 033109: 2′- deoxy-ACATCCCTGAACGA-CACa5;
Where 5: universal CPG & a: double coupling of the first base

Quality Assurance Highlights for Clinical Grade Phosphoramidites & Solid Supports

ChemGenes Phosphoramidites and Solid Supports have proven to be the Superior Source for GMP grade oligonucleotides

Key Applications:

- Applicable FDA Guidance for Q7A Good Manufacturing Practice for Active Pharmaceutical Ingredients for the intermediates used for production of natural and modified DNA/RNA, manufactured at ChemGenes Corporation.
- Dedicated Quality Management Team in place.
- Full materials management for all materials.
- QA process in place to manage deviations and their investigation and CAPA steps.
- Batch Records maintained to include full documentation and records for process control and release or rejection (based on acceptable criteria) of intermediates and final products.
- The Analytical methods for developing Release Specifications for the determination of identity and purity include Control Charts for optical rotation, 31P-NMR, 1H-NMR, ESI/MS, HPLC, and UV Analysis.
- On-going Stability Studies for key phosphoramidites and intermediates used in oligonucleotide synthesis: storage conditions of samples are described and analytical data at various time points are available.

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RNA Synthesis — Reverse Direction

Phosphoramidites for Reverse RNA Synthesis

RNA synthesis in 5′»3′ — direction

Coupling Efficiency approaching 99% makes this approach highly useful.

Key Applications:

- Highly efficient synthesis of synthetic RNA in the Reverse direction.
- Application in convenient introduction of Ligands, chromphores and modifications of Synthetic RNA at the 3′— End.
- Design of Sense Strand of SiRNA
- Challenging 3′ — Modifications of RNA

Structural Features:

The reverse RNA monomer phosphoramidites carry a 3′— DMT group, 2′– tBDsilyl (tBDSi) or 2′— triisopropylsilyloxymethoxy (TOM) and 5′— cyanoethylphosphoramidite (CED) group.

Quality Control:

- HPLC Purity of 98% and greater
- 31 P NMR purity from 98 – 100%
- Coupling Efficiency approaches 99% per step.

Patent Pending by ChemGenes Corp.

RNA Synthesis with TOM Phosphoramidites

TOM products are licensed from Qiagen Inc. for Therapeutic market

Key Advantages:

- Superior Quality RNA using 2′-O- TOM protection: No possibility of 2′– 5′— linkage
- Perfected manufacturing process: prices comparable to TBDMS
- Higher Coupling Efficiency due to lower steric hindrance: Reduced Coupling Time (2 – 4 minutes)
- No base modification or M + 30 observed (extensive chemical Ionization mass analysis)

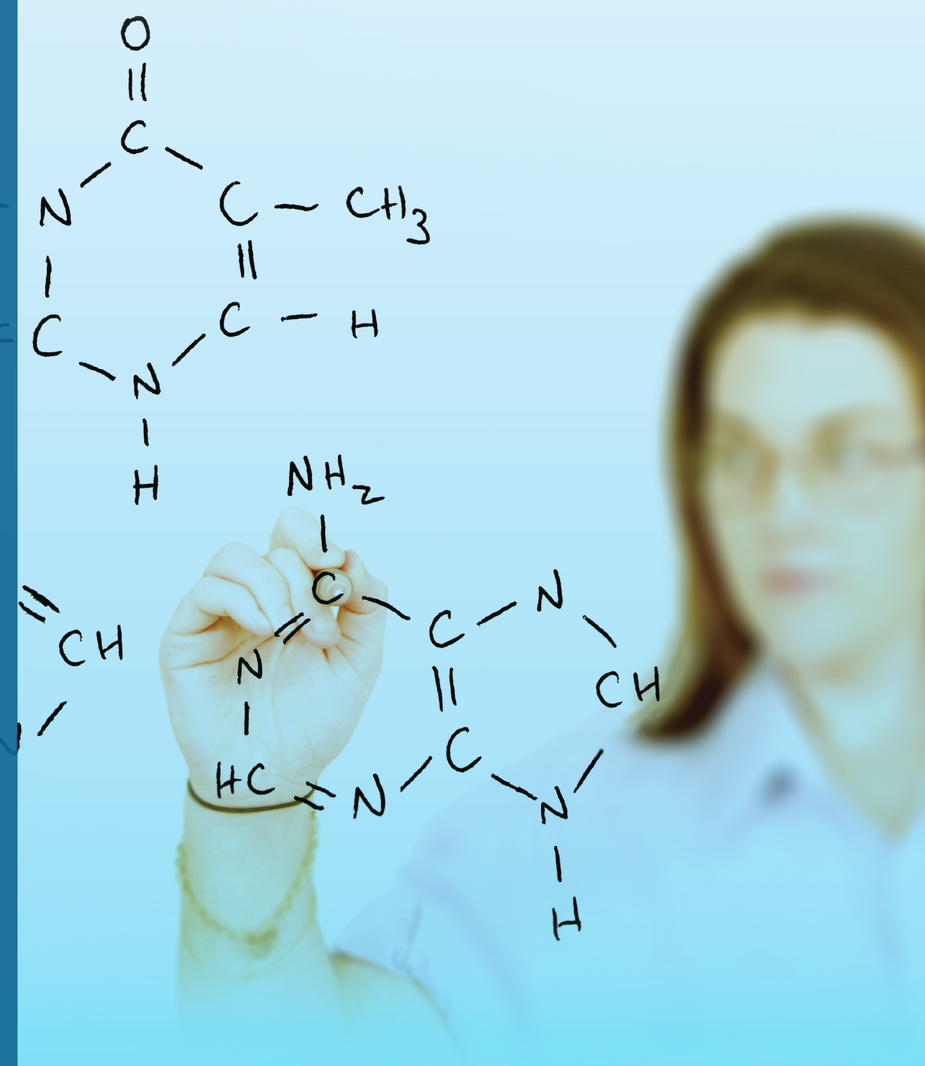
Quality Guaranteed:

- Purity Greater than 97% by HPLC
- 31 P NMR purity ranges from 98 –100%
- UV Spectral data to conform to highest
- 1 H NMR data to conform
- Coupling efficiency greater than 98% per step
- Ideal for Long Chain Oligos
- TOM Amidites Produced under GMP guidelines

Also Available:

Low to high loading CPG supports with TOM-monomer for uniform deprotection of RNA's.

Now Available Bulk Quantities Manufactured Under GMP Guidelines



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