ChemGenes CORPORATION

Exceptional Quality Products for Drugs and Diagnostics

- **Natural 2′-O-TBDMS-RNA Phosphoramidites**
  Standard Base Protection
  2′-O-TBDMS-A^{Bz}
  2′-O-TBDMS-C^{Ac}
  2′-O-TBDMS-G^{iBu}
  2′-O-TBDMS-U

  Mild Base Protection
  (N-Acetyl protection)
  2′-O-TBDMS-A^{Acetyl}
  2′-O-TBDMS-C^{Acetyl}
  2′-O-TBDMS-G^{Acetyl}

  Ultra Mild Base Protection
  (N-Pac protection)
  2′-O-TBDMS-A^{Pac}
  2′-O-TBDMS-C^{Pac}
  2′-O-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′-Fluoro-RNA Phosphoramidites**
  2′-fluoro-A^{Bz}
  2′-fluoro-C^{Ac}
  2′-fluoro-G^{iBu}
  2′-fluoro-U

- **2′-Fluoro-RNA Phosphoramidites (Mild Deprotecting groups)**
  2′-fluoro-C^{Ac}
  2′-fluoro-C^{Fmoc} [Patent Pending]
  2′-fluoro-G^{Ac} [Patent Pending]

Quality of our 2′-Fluoro phosphoramidites: HPLC > 98%; ^{31}P 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-ACATCCCTGAACGACACa5;
Where 5: universal CPG & a: double coupling of the first base

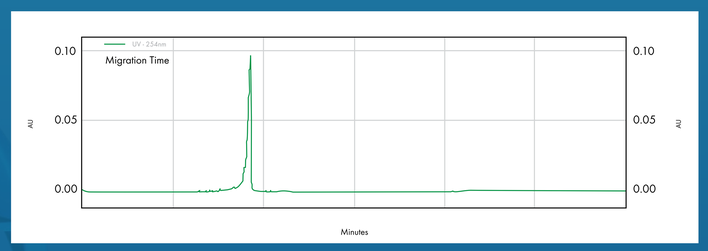

Fig. 1: CE Analysis: DNA Oligo seq # 033109 - synthesized with Unylinker CPG

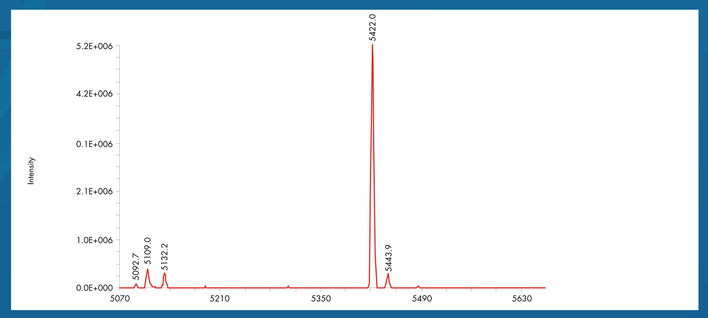

Fig. 2: ESI/MS report: DNA Oligo seq # 033109 – synthesized with Unylinker CPG
Calculated Mass: 5421.6
Observed mass: 5422.07, 5443.99 (M+Na); Observed mass: 5109.0(N-1), 5132.2 (N-1+Na).

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

- **Ongoing Quality Assurance Development Program towards FDA Q7A Good Manufacturing Practice** 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, ^{31}P-NMR, ^{1}H-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)

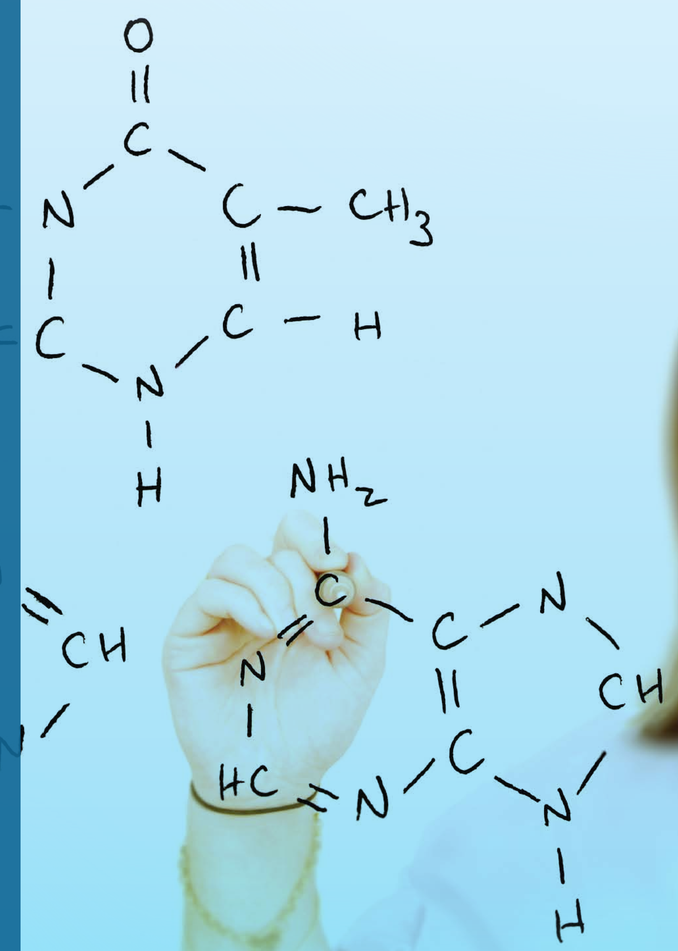
Quality Guaranteed:

- 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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