



OLIGONUCLEOTIDE CUSTOM SYNTHESIS

www.trilinkbiotech.com

 **TriLink**
BioTechnologies
The Modified Nucleic Acid Experts

Custom Synthesis

The Art of Fine Oligonucleotides Mastered

With our expertise and extensive selection of dyes, quenchers, modified bases, linkers, spacers and conjugates, your creativity is the limit. TriLink specializes in challenging constructs such as oligonucleotides with numerous modifications, molecular beacons and probes with multiple labels.

Consistently producing unique, superior grade oligonucleotide probes is an art form. Automated systems cannot recognize the nuances of distinct sequences and dye sets. Our skilled technicians isolate each compound using protocols designed to ensure we deliver the highest purity and yield for each oligonucleotide. By employing a hands-on approach, we offer a scalable process with unsurpassed quality and exceptional value.

All of these reasons make us a natural choice for oligonucleotide kit suppliers and testing facilities, as well as pharmaceutical, biotech and academic researchers.

- Extensive Customization Abilities
- Excellent Customer Service

- Expert Technical Support
- Scalable Processes

How to Order

We ask that all oligonucleotide sequences be submitted electronically through OligoBuilder®, our online ordering system, or by email to ensure accuracy. Please be sure to include your sequence, backbone, any modifications and synthesis scale or final yield. We accept payment by purchase order, wire transfer and credit card (MasterCard, Visa and American Express). To request a formal quotation, please go to www.trilinkbiotech.com/products/oligo/quote.asp. Visit our website for new products and technical resources.

☎ Phone 800-863-6801

☎ Fax 858-546-0020

🌐 Online www.trilinkbiotech.com

@ Email sales@trilinkbiotech.com

Expert Technical Support

The TriLink Team is committed to fully supporting TriLink's products and services from the initial customer inquiry to post delivery technical assistance. The answers to many common questions can be found online in our FAQ database. Have a unique question? Visit our *Ask An Expert* blog. Our technical support team is also available to speak with you Mon-Fri, 7 am to 5 pm PT.

Resources

TriLink offers a number of technical resources to aid in your research efforts. The following technical resources are available at www.trilinkbiotech.com.

- Ask An Expert blog
- Product line bibliography
- Publications
- FAQ database
- Literature corner
- Technical Articles



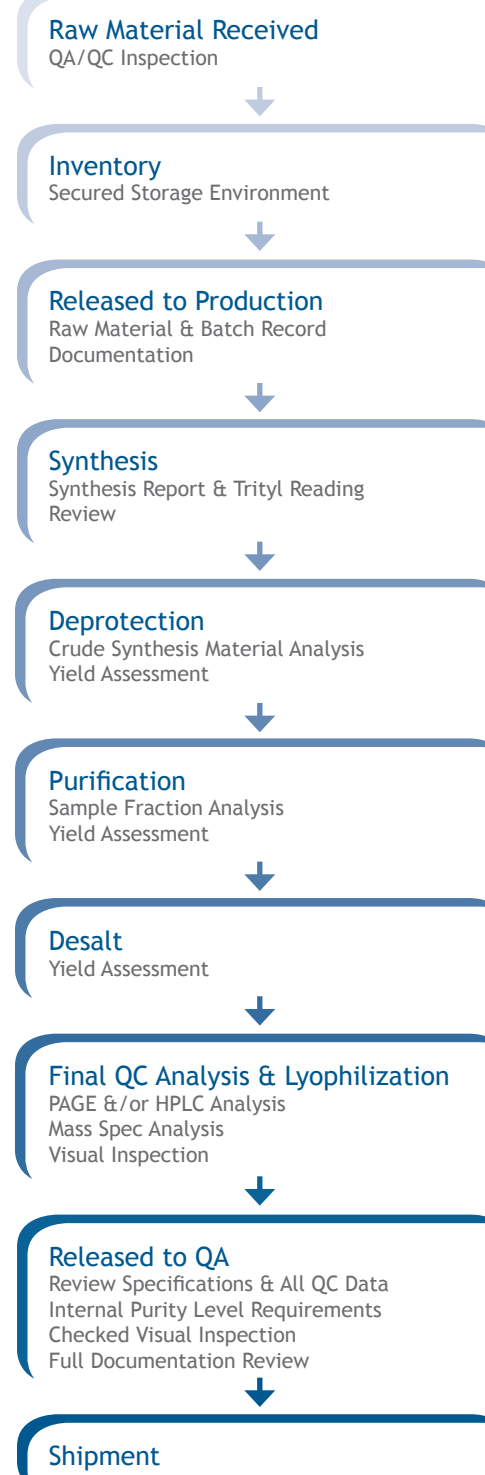
ResearchRewards Program

TriLink offers ResearchRewards to help offset the cost of nucleic acid-based products to support educators and researchers. To apply, email a completed application to info@trilinkbiotech.com. Applications may be submitted anytime. Applicants will be notified of the review results within two months.

To download an application or learn more visit:
www.trilinkbiotech.com/about/researchrewards.asp

Signature TriLink Quality

Since 1996, TriLink has manufactured specialty modified oligonucleotides. Our strong quality commitment and our extensive experience with unique modifications results in the best oligonucleotides possible. Producing high quality oligonucleotides requires rigorous QC. Each oligonucleotide undergoes quality control analysis by PAGE, HPLC and/or MS. The flowchart below displays many of the steps and process control points we do to ensure you receive quality product. TriLink operates a fully GMP facility and is ISO 9001:2008 and FDA 21CFR 820 compliant.

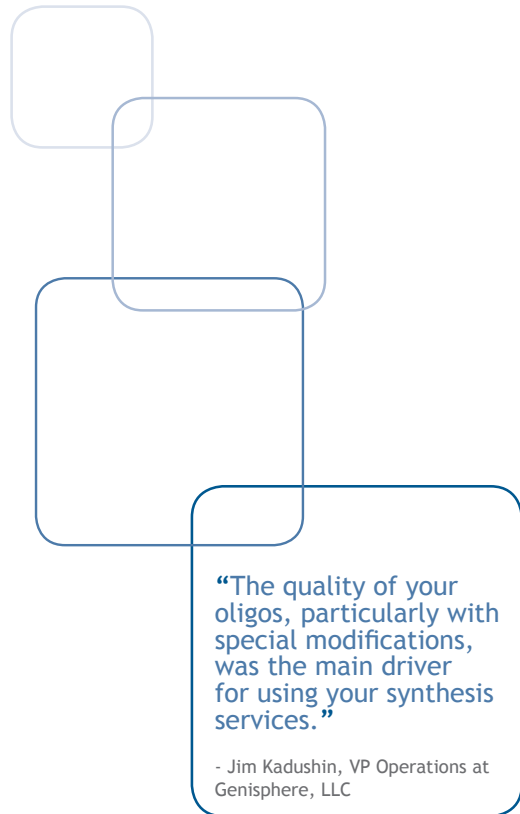


Customer Testimonials

“TriLink was willing to work with me to get the desired purity on a difficult synthesis.”
- Donald Hirsh, Associate Professor at The College of New Jersey

“I definitely found some products which others don't generally have. The customer service people I got in touch with have been very helpful in addressing my concerns and questions.”
- Yue Suo, Research Scientist at 454 Life Sciences

Building Your Oligonucleotide



1

Synthesis Scale or Final Yield

Use the chart below to determine the starting synthesis scale your project requires. Oligonucleotides may also be requested with a final yield.

2

Backbone

Choose your backbone. The Backbone Options table below will help you determine the linkage choices available for each sugar type.

3

Modifications

Determine the modifications required. See the Oligonucleotide Modification Guide on the opposite page for many of the dyes, modified bases and other modifications available. Don't see the modification you need? Please inquire. We can incorporate most commercially available modifications and also offer custom phosphoramidite synthesis.

4

Purification

Decide on a purification method. See our article *When is my Oligonucleotide Pure Enough?* to learn more about purity, analytical methods and purification options based on application. Not sure which purification method to choose? Simply request a quote and indicate "Best Method" or ask our technical support team.

Synthesis Scales		Final Yields	Backbone Options				Purification Methods
Starting Scale	Expected Yield**	1 mg ↓ 10 g	Backbone	PO	PS	MP	Desalt Only Primer Cartridge* RP-Cartridge Single RP/AX-HPLC Double RP/AX-HPLC PAGE PAGE & RP/AX-HPLC
40 nmole*	3 OD ₂₆₀		DNA	✓	✓	✓	
0.2 μmole	5-15 OD ₂₆₀		2' OH RNA	✓	✓	N/A	
1.0 μmole	20-60 OD ₂₆₀		2' OMe RNA	✓	✓	N/A	
15 μmole	300+ OD ₂₆₀		2' Fluoro RNA	✓	✓	N/A	
*Only available for primer grade material. **Expected yields are affected by each step in the manufacturing process, as well as modifications and sequence effects.		Standard pricing available for PO/PS DNA 15-25 bases, 50 mg - 10 g. For all other quantities and constructs, please request a quote.	PO = Phosphodiester PS = Phosphorothioate MP = Methylphosphonate				*Only available for primer grade material.

Online Ordering

Most oligonucleotide constructs can be priced and ordered directly through our custom oligo online ordering system, OligoBuilder®. The benefits of OligoBuilder® include instant pricing on highly modified oligonucleotides and reduced turnaround time. Visit www.oligobuilder.com.

Quotations

If your project requires bulk quantities, modifications not listed in OligoBuilder® or process development, please submit a quote request by visiting www.trilinkbiotech.com/products/oligo/quote.asp. Contact our technical support team with any questions you may have regarding your oligonucleotide.

OligoBuilder®

Oligonucleotide Modification Guide

TriLink specializes in highly modified oligonucleotides. Whether you are interested in dyes, quenchers, linkers, spacers or modified bases, we can work with you to synthesize the right oligonucleotide for your project. Below are the most common oligonucleotide modifications.

Don't see what you need? Just Ask!

Fluorescent Labels	Modified Bases	Etheno-2'-deoxyadenosine
6-FAM (Fluorescein) (6-Carboxyfluorescein)	2',3'-Dideoxyadenosine	Inosine
6-JOE	2',3'-Dideoxycytidine	K-2'-deoxyribose
7-Aminocoumarin-X (AMCA-X)	2',3'-Dideoxyguanosine	N4-Ethyl-2'-deoxycytidine
7-Methoxycoumarin	2',3'-Dideoxythymidine	N6-Methyl-2'-deoxyadenosine
Alexa Fluor® 350	2,6-Diaminopurine	O4-Methylthymidine
Alexa Fluor® 405	2,6-Diaminopurine-2'-deoxyriboside	O6-Methyl-2'-deoxyguanosine
Alexa Fluor® 430	2,6-Diaminopurine-2'-O-methylriboside	O6-Phenyl-2'-deoxyinosine
Alexa Fluor® 488 (mixed isomers)	2-Aminopurine	P-2'-deoxyribose
Alexa Fluor® 514 (mixed isomers)	2-Aminopurine-2'-deoxyriboside	P-2'-deoxyribose
Alexa Fluor® 532	2-Aminopurine-2'-O-methylriboside	Pseudouridine
Alexa Fluor® 546	2'-Deoxyinosine	Puromycin
Alexa Fluor® 555	2'-Deoxyisoguanosine	Pyrrolo-2'-deoxycytidine
Alexa Fluor® 568 (mixed isomers)	2'-Deoxynebularine	Pyrrolocytidine
Alexa Fluor® 594 (mixed isomers)	2'-Deoxypseudouridine	Thymidine Glycol
Alexa Fluor® 610	2'-Deoxyuridine	Biotin & Other Non-fluorescent Conjugates
Alexa Fluor® 633	2'-O-Methylinosine	Biotin BB
Alexa Fluor® 647	2-Thiothymidine	Biotin
Alexa Fluor® 660	3-Deaza-5-aza-2'-O-methylcytidine	Biotin TEG
Alexa Fluor® 680	3'-Deoxyadenosine	Biotin-dT
Alexa Fluor® 700	3'-Deoxycytidine	Biotin Diol Linker
Alexa Fluor® 750	3'-Deoxyguanosine	Dual Biotin
BODIPY-493/503™	3'-Deoxythymidine	PC Biotin
BODIPY-558/568™	3-Nitropyrrole-2'-deoxyribose	Cholesteryl TEG
BODIPY-530/550™	4-Thio-2'-deoxyuridine	DNP-X
BODIPY-564/570™	4-Thiothymidine	DNP TEG
BODIPY-576/589™	4-Thiouridine	Psoralen C2
BODIPY-581/591™	5-(C2-EDTA)-2'-deoxyuridine	Psoralen C6
BODIPY-TR-X™	5-(Carboxy)vinyl-2'-deoxyuridine	Acridine
CAL Fluor® Gold 540	5,6-Dihydro-2'-deoxyuridine	Abasic
CAL Fluor® Orange 560	5,6-Dihydrothymidine	Linkers
CAL Fluor® Red 590	5'-Aminothymidine	3' C3 Amino Linker
CAL Fluor® Red 610	5-Bromo-2'-deoxycytidine	3' C6 Amino Linker
CAL Fluor® Red 635	5-Bromo-2'-deoxyuridine	3' C7 Amino Linker
Carboxynaphthofluorescein (5 & 6 mixed esters)	5-Bromo-2'-O-methyluridine	5' C6 Amino Linker
Carboxyrhodamine 6G™	5-Bromouridine	5' C12 Amino Linker
Carboxy-X-Rhodamine™ (X-Rhodamine, ROX)	5-Fluoro-2'-deoxycytidine	PC Amino Linker
Cascade Blue™	5-Fluoro-2'-deoxyuridine	3' C3 Disulfide Linker
Cy3.5™	5-Fluoro-2'-O-methyluridine	3' C6 Disulfide Linker
Cy3™	5-Fluoro-4-O-TMP-2'-O-methyluridine	Aldehyde
Cy5.5™	5-Hydroxy-2'-deoxycytidine	Carboxy-dT Linker
Cy5™	5-Hydroxy-2'-deoxyuridine	DADE Linker (5' Carboxyl Linker)
Dansyl-X	5-Hydroxymethyl-2'-deoxycytidine	Thymidine-5-C2 and C6 Amino Linker
Dimethylaminocoumarin®	5-Hydroxymethyl-2'-deoxyuridine	2'-Deoxyadenosine-8-C6 Amino Linker
DTAF	5-Iodo-2'-deoxycytidine	2'-Deoxycytidine-5-C6 Amino Linker
dT-FAM	5-Iodo-2'-deoxyuridine	2'-Deoxyguanosine-8-C6 Amino Linker
dT-TAMRA	5'-Iodothymidine	C7 Internal Amino Linker
HEX (Hexachlorofluorescein)	5-Iodouridine	PC Linker
Marina Blue®	5-Methyl-2'-deoxycytidine	Spacers
NBD-X	5-Methyl-2'-Deoxyisocytidine	C3 (Propyl) Spacer
Oregon Green 488™	5-Methyl-2'-O-methylcytidine	C6 Spacer
Oregon Green 514™	5-Methyl-2'-O-methylthymidine	Spacer 9 (Triethylene glycol; PEG-150)
P130	5-Methylcytidine	C12 Spacer
Pacific Blue®	5-Methyluridine	Spacer 18 (Hexaethylene glycol; PEG-282)
PyMPO	5-Nitroindole-2'-deoxyriboside	dSpacer
Quasar® 570	5'-O-Methylthymidine	rSpacer
Quasar® 670	5-Propynyl-2'-deoxycytidine	PC Spacer
Rhodamin Green-X™ (mixed isomers)	5-Propynyl-2'-deoxyuridine	Terminal Phosphates
Rhodamine Red-X™	6-O-(TMP)-5-F-2'-deoxyuridine	5' Phosphate
TAMRA-X	6-Thio-2'-deoxyguanosine	3' Phosphate
TET (Tetrachlorofluorescein)	7-Deaza-2'-deoxyxanthosine	5' Thiophosphate
Texas-Red-X™ (mixed isomers)	7-Deaza-2'-dexoyadenosine	3' Thiophosphate
Quenchers	7-Deaza-2'-deoxyguanosine	Inverted Oligonucleotides
3'-DABCYL CPG	7-Deaza-8-aza-2'-deoxyadenosine	3'-3' Modifications
Black Hole Quencher 1®	8-Amino-2'-deoxyadenosine	5'-5' Modifications
Black Hole Quencher 2®	8-Amino-2'-deoxyguanosine	Trimer Oligonucleotide Synthesis
DABCYL SE (Carboxamide linker)	8-Bromo-2'-deoxyadenosine	Cis-Syn Thymidine Dimer
DABCYL-dT	8-Bromo-2'-deoxyguanosine	
QSY-21®	8-Oxo-2'-deoxyadenosine	
QSY-35®	8-Oxo-2'-deoxyguanosine	
QSY-7®	Aracytidine	
QSY-9®	C4-(1,2,4-Triazol-1-yl)-2'-deoxyuridine	

Oligonucleotides for Diagnostics / OEM

Designing and developing specifications for your diagnostic kit components can be an impossible challenge without a nucleic acid chemist on your team. Since 1996 we have been applying our unique nucleic acid chemistry expertise to our customers' technical barriers.

Your Perfect Partner

We will work closely with you to tailor the manufacturing process to your specific program needs. Our extensive research in randomization optimization for the Roche NimbleGen microarrays is a great example of how we can make your product even better. Our process development and scale-up research in support of the Applied Biosystems SOLiD™ System oligonucleotides is another example of what our technical expertise can do for you. To learn how our ingenuity can work for you, please contact our technical support team.



A Customized Program

Whether you are ordering your first oligonucleotide or are ready to set up a full supply program, TriLink is the right supplier for you. Material can be ordered in nmoles all the way up to multiple grams. We offer several levels of purification to meet your needs. Our crude material ranges from 60% - 80% pure. We will not ship any purified material unless it meets our 85% purity minimum without your request and approval. Greater purity can be achieved with additional purification steps at your request.

QC Analyses Available

- PAGE analysis & gel densitometry
- Mass spectroscopy
- RP/AX-HPLC analysis
- Synthesis report
- Other assays available

Additional Services Available

- Custom labeling & documentation
- Research & development
- Manufacturing process optimization
- Controlled access to dedicated laboratories

QSR Manufacturing

Every product made at TriLink is manufactured under QSR, whether it is for diagnostics, therapeutics or research. At TriLink our top priority has always been manufacturing the highest quality products for our customers. We will work with you to develop, document and validate processes and materials for your specific program. We will then manufacture your product under a quality system based on the FDA's Quality System Regulations (QSR) and the ISO 9001:2008 standard. We also offer programs compliant with the FDA 21CFR 820 regulation for ASR manufacturing.

Benefits of Manufacturing under QSR:

- Manufacturing process validation
- Optimized synthesis & purification protocols
- Locked process & specification documentation
- Separate batch record for each compound
- Dedicated program review
- Final product labeling line clearance

Program Guidelines Include:

- All personnel trained in QSR compliance
- SOPs & central records handling
- Supplier validation & traceable raw material

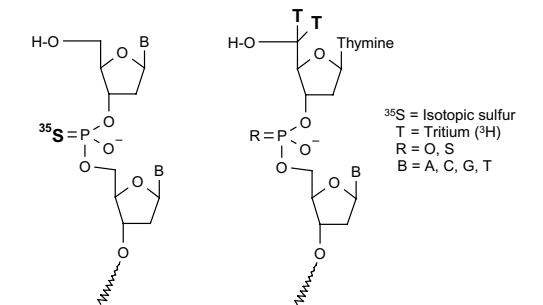
Contact Us to Discuss Your Project Today!

Oligonucleotides for Therapeutics

TriLink specializes in mid-scale synthesis of both DNA and RNA oligonucleotides. We understand how important the material required for pre-clinical, diagnostic and therapeutic studies is to our customers. Our pricing is very competitive and we are committed to providing the highest quality products. We offer quantities from 50 mg to 10 g. If you require more than 10 g, we recommend our alliance partner Avecia. All products are analyzed by PAGE, HPLC and MS. Turn around time varies based on sequence, purification and quantity requested. Please inquire. Additional services available include modifications, radioactive labeling, process development and cGMP and QSR manufacturing.

Radioactive Labeling

TriLink offers ³⁵S and ³H labeling of phosphodiester and phosphorothioate oligonucleotides. Radioactively labeled oligonucleotides are often required by the FDA for an IND (investigative new drug) filing, which is an early step in the process of drug approval. Our compounds are prepared manually and HPLC purified to greater than 90% full length product to ensure the highest quality. Our process typically yields greater than 95% radio-isotopically pure material. Our extensive experience in preparing radioactively labeled oligonucleotides specifically for pre-clinical trials ensures you will receive a superior product.



RNA Oligonucleotides and Other Therapeutic RNAs

Over the last two decades, there has been significant progress in the development of oligonucleotides as therapeutics. RNA and DNA oligonucleotides have been used as antisense inhibitors, aptamers, CpG immunostimulatory molecules, molecular decoys and as RNA interference (RNAi) triggers. Antisense therapeutics are currently experiencing a renaissance, with very promising results in preclinical studies in non-human primates and in human clinical trials.

RNAi is a phenomenon in which the introduction of double-stranded RNA into a cell results in sequence-specific gene silencing. RNAi is a powerful research tool and a promising new class of potential therapeutics. Investigations into the mechanisms of RNAi have led to the discovery of microRNAs, which are thought to regulate about half of all genes. Oligonucleotide based microRNA mimics and inhibitors are exciting new therapeutic research tools. Aptamers are also showing promise as therapeutics in animal models and are likely to be useful in the field of proteomics.

TriLink is a key supplier of RNA and DNA oligonucleotides for pre-clinical research. We specialize in highly modified oligonucleotides, including RNA and derivatives such as 2' O-Methyl RNA, 2' Fluoro RNA, as well as thioated versions and conjugation to molecules such as PEG and cholesterol. We are here to support your therapeutic research through our expertise in high quality nucleic acid synthesis and modification.

Custom mRNA Synthesis

TriLink is proud to announce the addition of a new service, custom messenger RNA (mRNA) and long RNA synthesis. Recently, capped and polyadenylated mRNA has gained attention as a tool for reprogramming stem cells, transiently expressing zinc-finger nucleases and as a potential therapeutic. Please contact us today to discuss your project.

The Avecia-TriLink Alliance

From discovery to the clinic

With over 130 clinical trials and 30 years combined experience in manufacturing, the Avecia-TriLink Team is the leader in therapeutic oligonucleotide technology and program development.

TriLink and Avecia have shared technology platforms, analytical methods, protocols and material samples to ensure a faster and easier scale-up of your compound. This harmonization allows the material you use in the clinic to more accurately represent the material used in pre-clinical investigations. This scale-up solution offers you more regulatory simplicity, less risk, as well as savings in time and costs.

www.trilinkbiotech.com/alliance
www.aveciabiotech.com

- Accelerate Product Commercialization
- Facilitate the Transition from Discovery to Clinical Trials
- Reduce Manufacturing Risks
- Achieve Reproducibility Throughout Scale-up

TriLink BioTechnologies is an industry leader in manufacturing high quality oligonucleotides and nucleoside triphosphates at small and mid-scales.

TriLink operates a GMP laboratory with a QSR environment and provides:

- Milligram to multi-gram synthesis
- Highly-modified oligonucleotides and nucleosides
- Oligonucleotide radiolabeling services
- Custom chemistry
- Contract research services
- Industry-leading technical support

Follow Us



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Printed with Soy-Based Inks