



# Oligonucleotide

API manufacturing

 **SUMITOMO CHEMICAL COMPANY, LIMITED**  
Pharmaceutical Chemicals Division

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 **SUMITOMO CHEMICAL**

# About Sumitomo Chemical

Sumitomo Chemical is a leading Japanese manufacturer and supplier of APIs and intermediates for the global pharmaceutical industry. By taking advantage of the experience accumulated over 40 years in the process development for APIs and intermediates, we are capable of establishing and managing the manufacturing process for high-quality oligonucleotides, amidites, and other raw materials.

## Services

### Manufacturing

Sumitomo Chemical has established the industrial manufacturing process for long RNA oligos that is capable of supplying quantities up to a few kilograms annually. Sumitomo Chemical supplies long RNA oligos that can be used for applications where purity and length are critical, such as genomic editing using the CRISPR Cas9 system, as well as nucleic acid therapeutics by siRNA, Aptamer, and ASO.

#### Categories



For nucleic acid therapeutics  
siRNA, Aptamer, ASO, etc.



For gene editing of  
tracrRNA, sgRNA, etc.

#### Quantities



Small-scale sample  
(milligrams to grams)



Large-scale production  
(several hundred grams to  
kilograms annually)



GMP and non-GMP  
manufacturing

### Development Support

Sumitomo Chemical lends extensive support to the development work by developing analytical methods, performing stability studies, and providing regulatory support, which results in a competitive advantage for its customers throughout the product life cycle.

#### Chemical Development

- Process development and optimization
- Scale-up
- Process validation

#### Analytical Method Development and Validation

- High-resolution separation method by UHPLC
- Accurate molecular weight determination (RNA : up to ~100 mer)
- Sequence determination by LC-MS/MS
- Structural analysis of impurities (Product-related and process-related impurities)

#### Regulatory Support

- A long track record of registering Drug Master Files (DMF)

#### Supplier Management

- Amidites
- Other starting materials
- Reagents

## Project Management

For project success, we assign each of our customer's project to competent project managers. Our project management team builds an optimal schedule through discussion with our customers about the technical problems and the tasks priority to obtain the solutions.

Our office in Brussels, Belgium, handles commercial inquiries in Europe and the US.

We set up regular video conferences between our customers and our R&D and production facilities in Japan to follow up on the progress and exchange information.

Sumitomo Chemical Europe  
S.A./N.V.

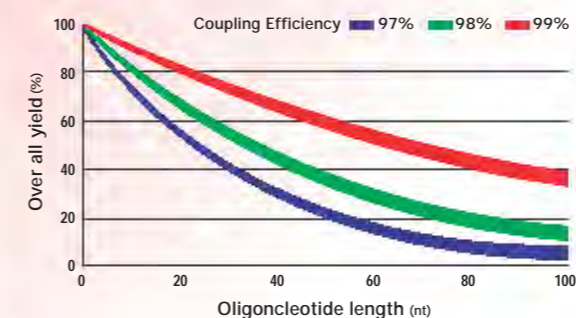
Sumitomo Chemical Co., Ltd.  
R&D and Manufacturing

# Technologies

## Oligo Synthesis

### Conventional Technology vs. Our Technologies - Yield

Only 1% difference in coupling efficiency can result in a huge impact on the overall yield of oligo products, as shown below.

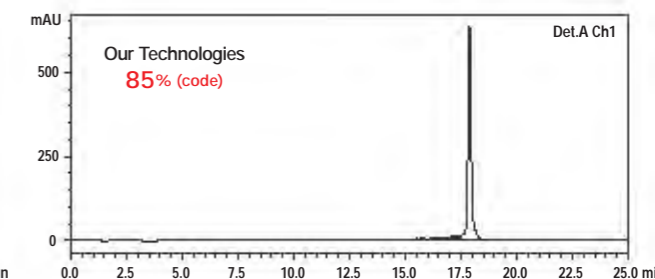
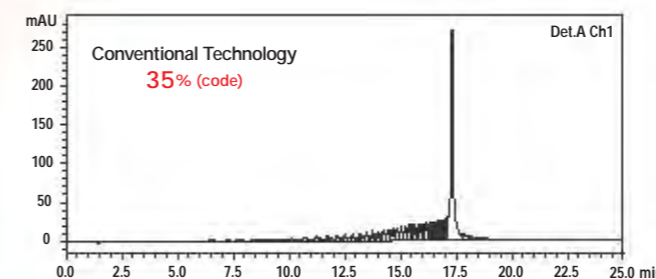


Sumitomo has developed unique synthetic technologies that render higher single coupling yield than conventional technologies to obtain high-quality long RNA oligos with sufficient overall yield.

"Overall yield image of oligo synthesis based on coupling efficiency"

### Conventional Technology vs. Our Technologies - Quality

A synthetic example of a poly-U 50 mer of several grams is shown below. FLP can be obtained with a **CRUDE** purity of more than 80% even in 50 mer.

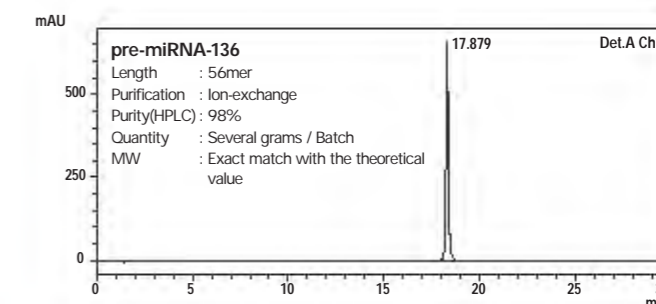


### Case Study : Synthetic Results of Long RNA oligos

Sumitomo Chemical has already established the industrial manufacturing process for long RNA oligos that is able to supply kilogram quantities annually. Examples are provided below.

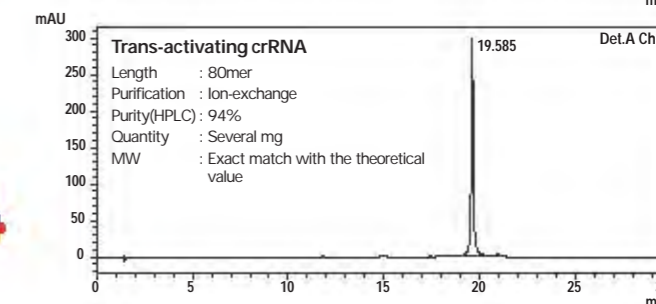
#### (a) Pre-miRNA

Pre-miRNA is a precursor of mature-miRNA, an RNA of approximately 60 bases long. The 56-mer Pre-miRNA 136 was synthesized with an HPLC purity of 99% with solid-phase synthesis using AKTA Oligopilot 100 and purified by column chromatography and lyophilization.



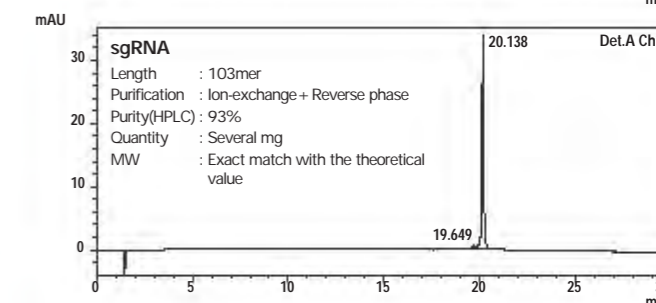
#### (b) Trans-activating crRNA

Trans-activating crRNA, 80 mer was synthesized with an HPLC purity of 94% with solid-phase synthesis using AKTA Oligopilot 100 and purified by column chromatography and lyophilization.



#### (c) sgRNA

sgRNA, 103 mer for the CRISPR Cas9 system was synthesized with an HPLC purity of 93% with solid-phase synthesis using AKTA Oligopilot 100. Sumitomo's procedure yielded over 90% purity even for over 100 mer sgRNA.



# *Oli-Go to the future.*

**Sumitomo Chemical offers reliable manufacturing services of high quality oligo:**

- From development to commercial stage/From mg to kg scale
- With unique high-yield coupling technologies
- Up to 100-mer with solid phase synthesis

**Including:**

- Process optimization & validation
- Analytical method development & validation
- Scale-up study/GMP production
- Supplier management
- Regulatory support