

# GETTING THE BEST OUT OF CYCLODEXTRINS

Technology presentation





**SUGAMMADEX**  
**THE FIRST CYCLODEXTRIN BASED API**

WHO ARE WE AT CYCLOLAB?



The world's only all-round **CYCLODEXTRIN** company with over  
**40-year experience of CD-technology**

**in pharmaceutical-, cosmetics-, food-, environmental- and analytical applications**

### Experience

over 490 technical/scientific papers  
and 950 technical reports to customers

200 different cyclodextrin derivatives  
130 patents/applications  
40 products on the market

Drug Master Files (USA type IV) and eCTD

Over 20,000 citations to CYCLOLAB's papers

### Expertise & Technology

Custom synthesis

Drug solubilization, and stabilization

Further industrial applications

Cyclodextrin-related analytics,

Stability testing

GMP-conform manufacturing

Feasibility studies



synthesis

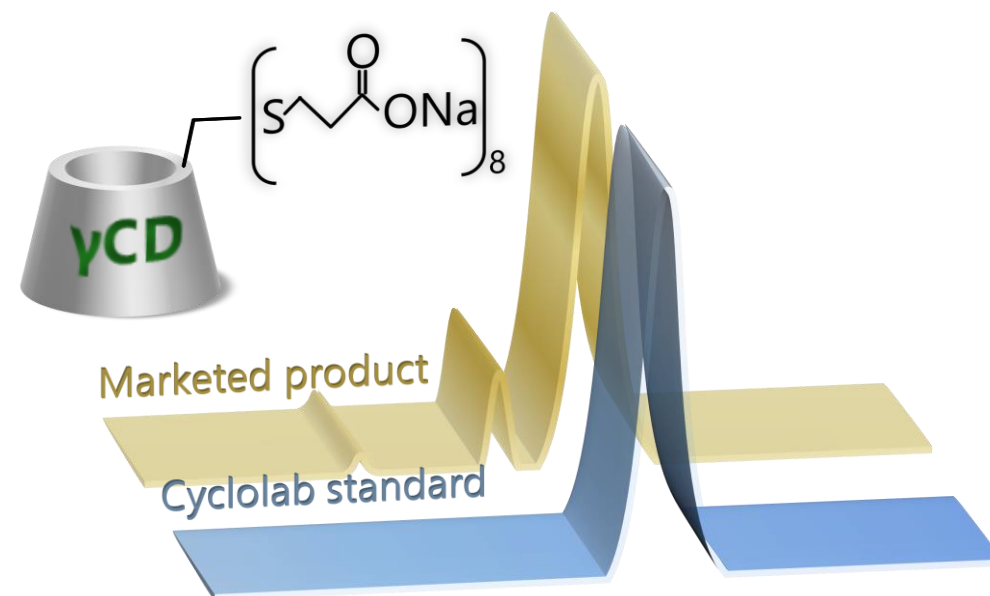
process and formulation development

contract analysis

IP/FTO search and evaluation

process intermediates

process impurities



## SUGAMMADEX BACKGROUND



Sugammadex (SGM) is one of the greatest successes in the history of cyclodextrins. There is an increasing interest for this product and for the development of Sugammadex, since the approval of Bridion, a blockbuster drug, by the FDA.

SGM is used in anesthesia as an injectable antidote for rocuronium and similar neuromuscular blocking agents.

CycloLab has vast experience in the production of Per-6-halogeno-gamma-CD intermediates and has developed Sugammadex via various process routes and related compounds, supported by sensitive analytical tools to characterize the products.



## SUGAMMADEX WHAT DOES CYCLOLAB OFFER?

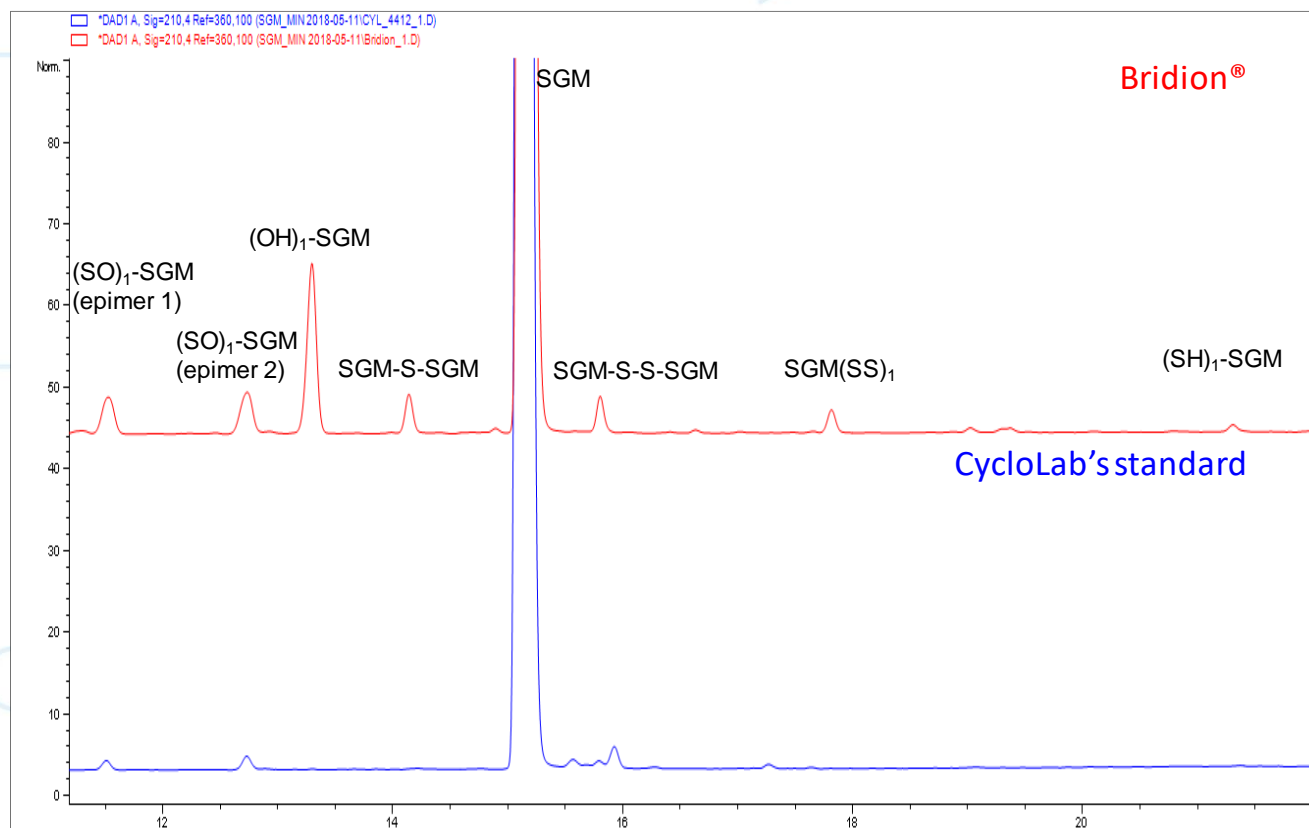


- Supplying the key intermediates (Per-6-halogeno-gamma-CDs) for the synthesis of the API (on commercial scale)
- Assisting in the optimization of the API production (from chemical and purification perspectives)
- Comparing samples (both API and final formulations) using sensitive analytical methods (capable of separating 20-30 potential impurities in the API)
- Providing high purity standards (intermediates, Sugammadex, key process impurities) to quantify the true and accurate purity of the compounds
- Providing formulation development and analytical services for the final product
- Conducting literature- and patent search for FTO/IP evaluation

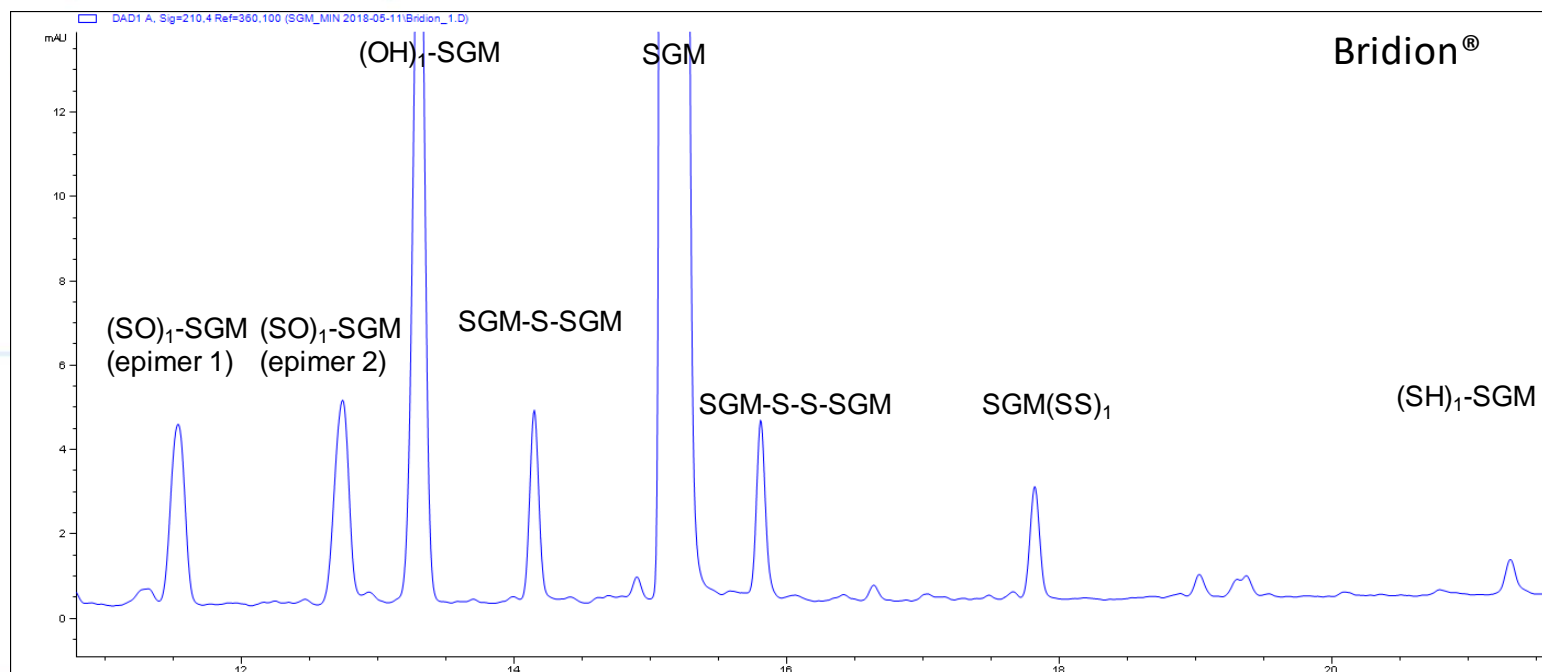


# SUGAMMADEX TECHNOLOGY AND ANALYSIS

Using CycloLab's technology, a standard material with exceptional quality outperforming the originator's in all aspects can be achieved.



Bridion® itself is claimed to potentially contain >20 cyclodextrin related impurities (public regulatory information), while other synthetic approaches generate just as many different ones. The accurate analysis of such an API is not possible without proper methods and standard materials.

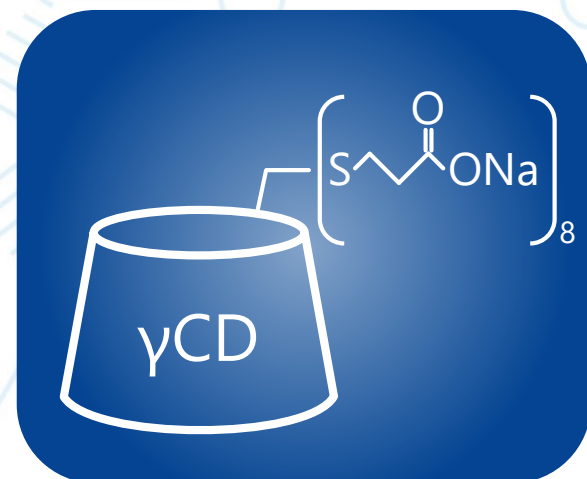


# SUGAMMADEX RAW MATERIAL AND PRODUCT STANDARDS



## Gamma-cyclodextrin Working Standard:

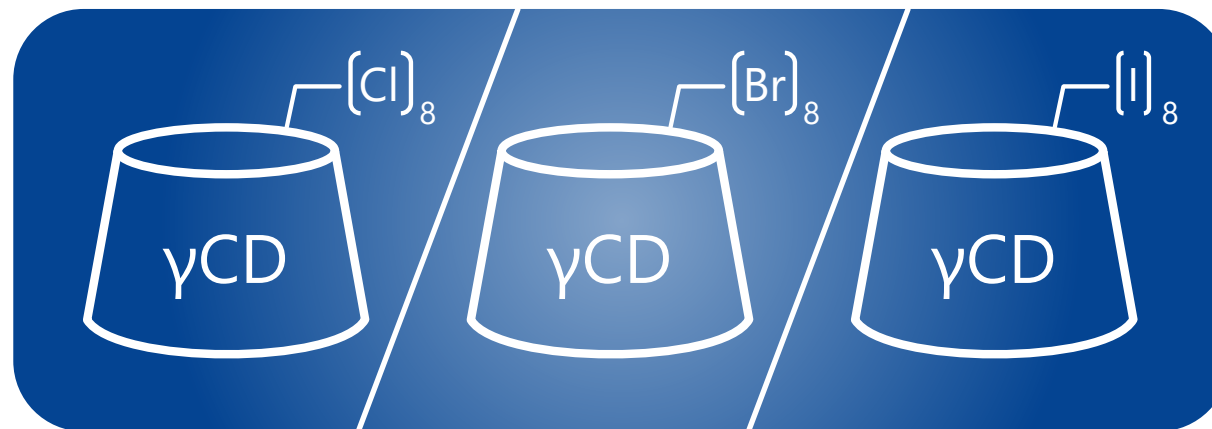
- Declaration by CycloLab



## Sugammadex Primary reference standard:

- >99.0% purity (on dry substance)
- Identification by NMR, IR, HPLC and HPLC-MS

## SUGAMMADEX PROCESS INTERMEDIATE STANDARDS



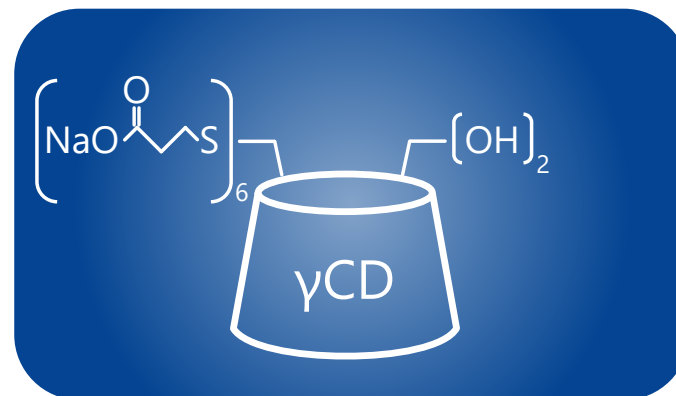
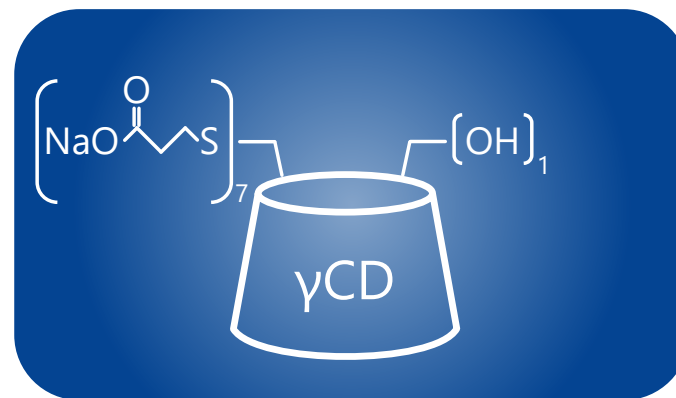
### Per-6-halogeno-gamma-cyclodextrin primary standards:

- Available for any chosen synthetic route (chloro-, bromo- or iodo derivative)
- >90% content
- Identification by NMR, IR

## SUGAMMADEX PROCESS IMPURITIES REGULARLY ON STOCK

### Mono-OH- and Di-OH-Sugammadex:

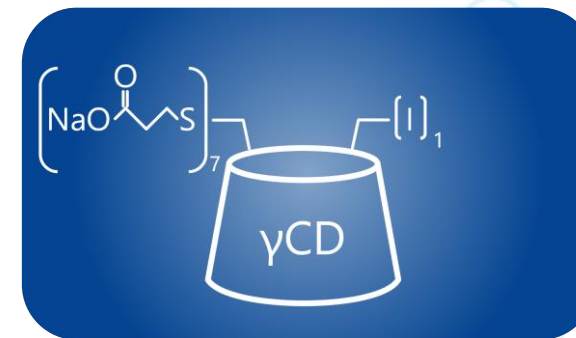
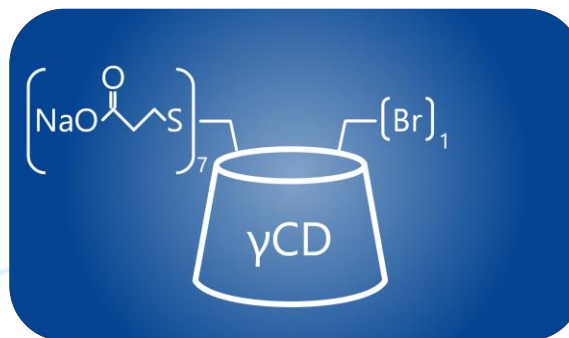
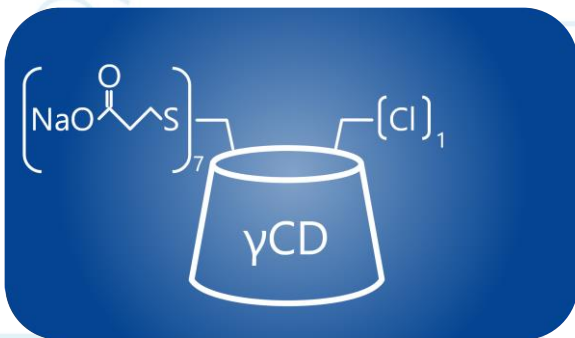
- >95% (Area%) with proprietary HPLC method, DAD detection, peak purity proven by LC-MS
- Identification by NMR, IR, HPLC-MS
- Residual solvents by TGM-MS and residual salts by CE



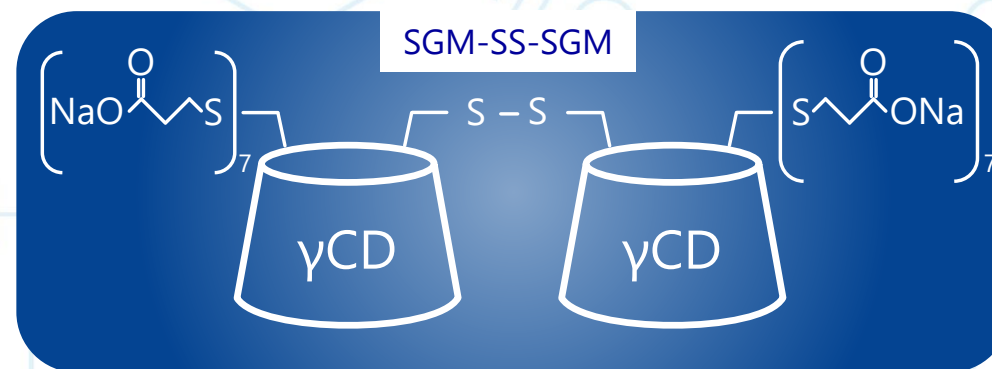
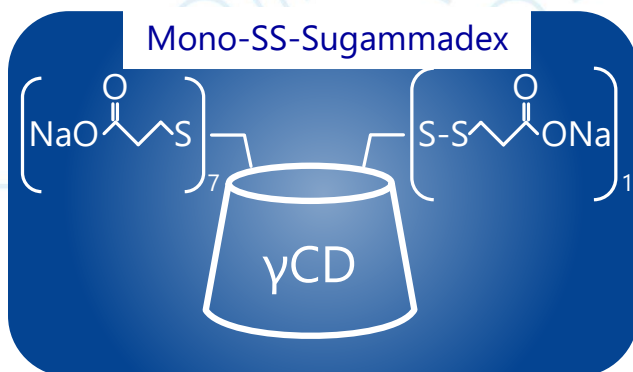
## SUGAMMADEX PROCESS IMPURITIES REGULARLY ON STOCK

### Mono-halogeno-Sugammadex:

- Available for all synthetic routes
- Minimum >90% (Area%) with proprietary HPLC method, DAD detection, peak purity proven by LC-MS
- Identification by NMR, IR, HPLC-MS
- Residual solvents by TGM-MS and residual salts by CE

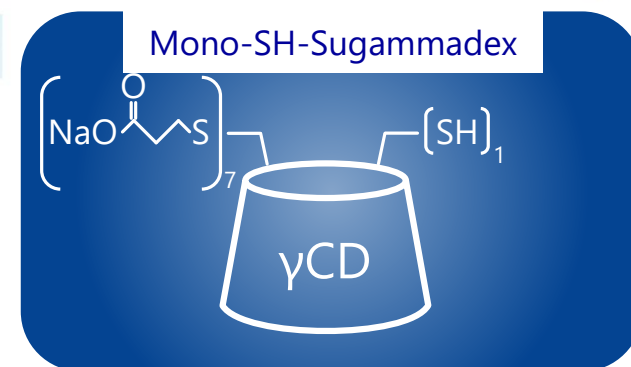
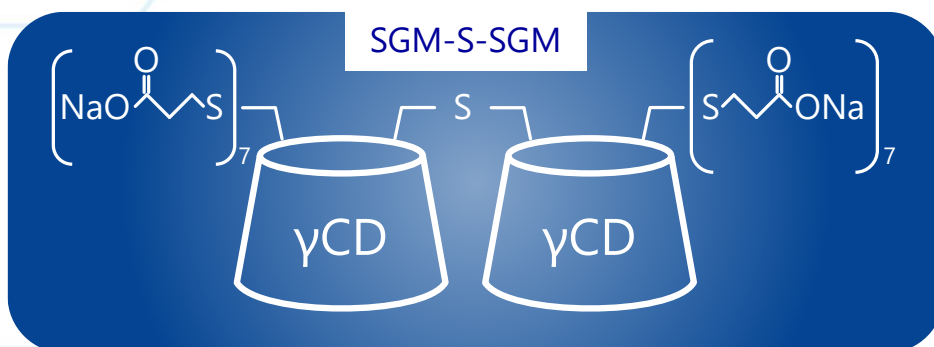


# SUGAMMADEX PROCESS IMPURITIES REGULARLY ON STOCK



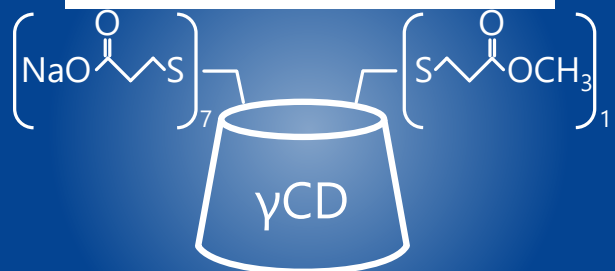
## Typical analysis:

- Minimum >90% (Area%) with proprietary HPLC method, DAD detection, peak purity proven by LC-MS
- Identification by NMR, IR, HPLC-MS
- Residual solvents by TGM-MS and residual salts by CE

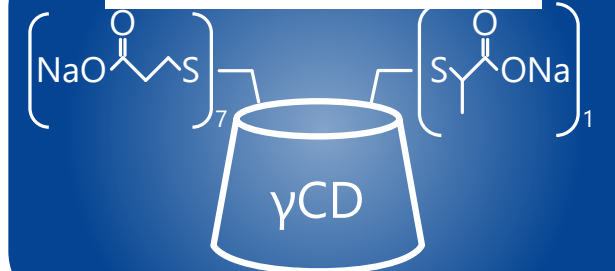


# SUGAMMADEX PROCESS IMPURITIES REGULARLY ON STOCK

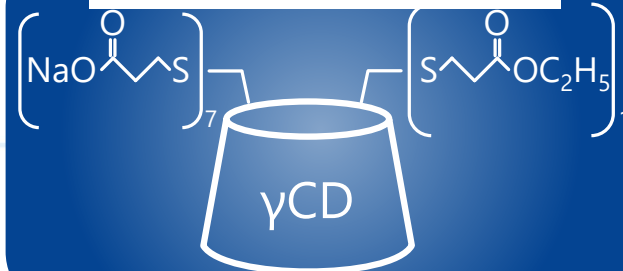
Mono-COOMe-Sugammadex



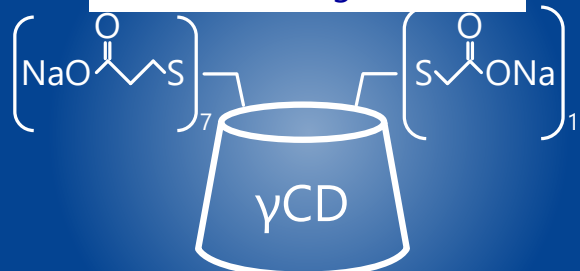
Mono-ISO-Sugammadex



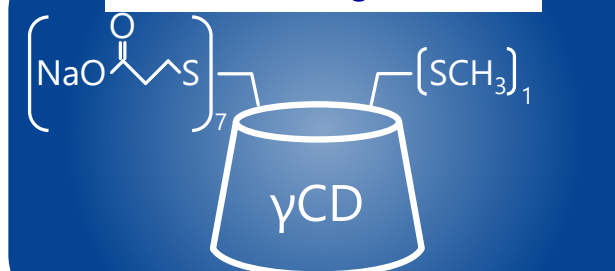
Mono-COOEt-Sugammadex



Mono-ACE-Sugammadex



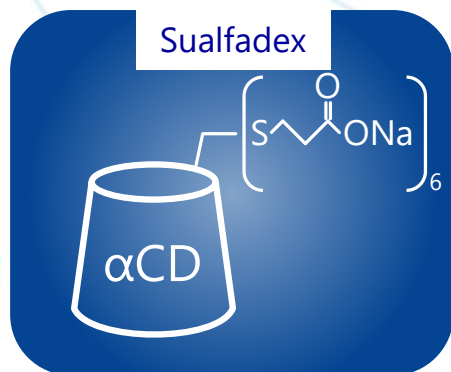
Mono-SMe-Sugammadex



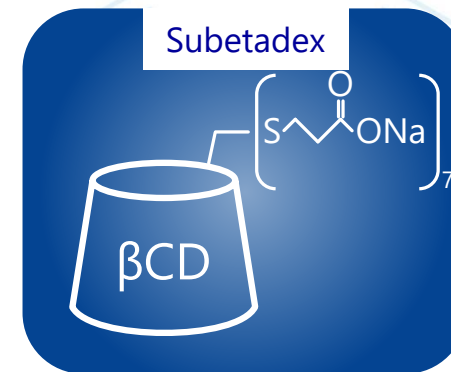
For typical analysis see slide 12

# SUGAMMADEX PROCESS IMPURITIES REGULARLY ON STOCK

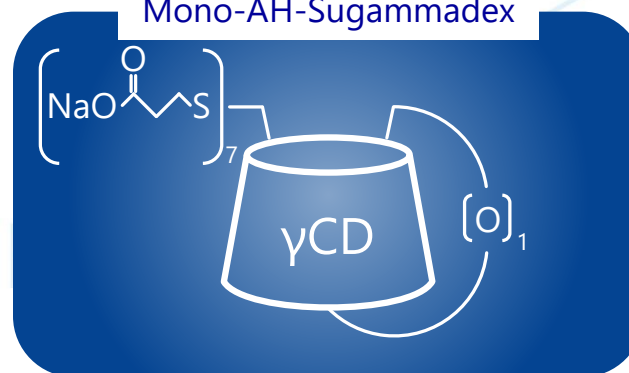
Sualfadex



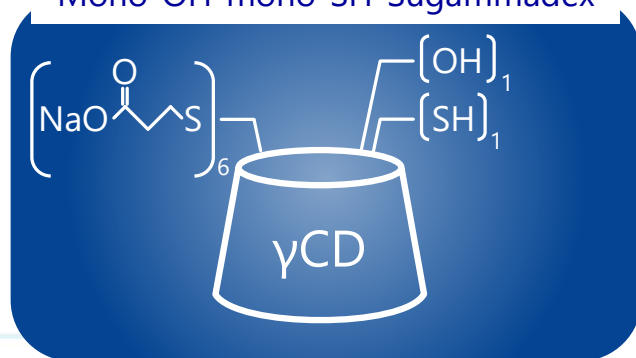
Subetadex



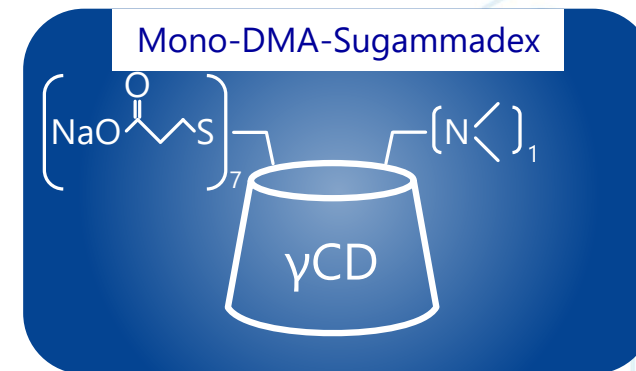
Mono-AH-Sugammadex



Mono-OH-mono-SH-Sugammadex



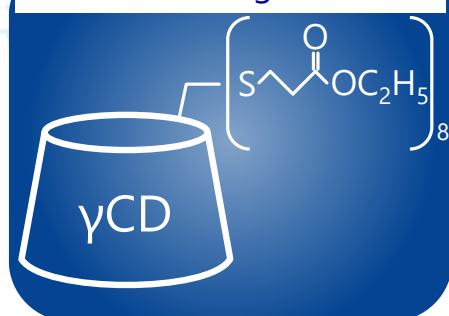
Mono-DMA-Sugammadex



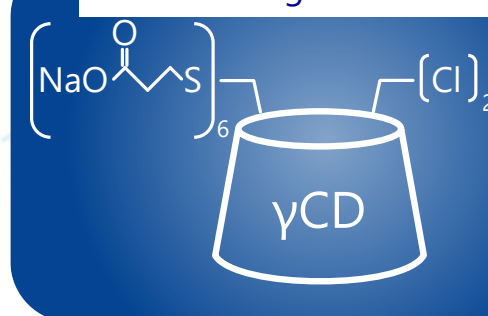
For typical analysis see slide 12

# SUGAMMADEX PROCESS IMPURITIES REGULARLY ON STOCK

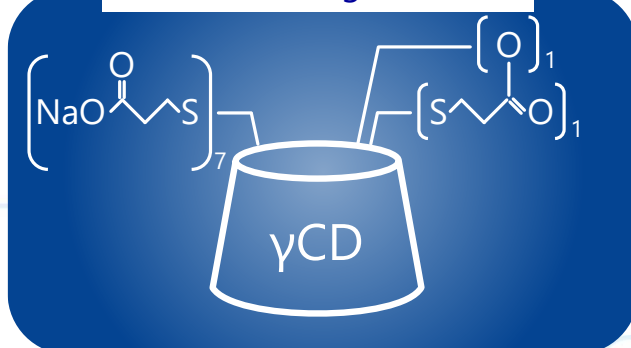
Per-COOEt-Sugammadex



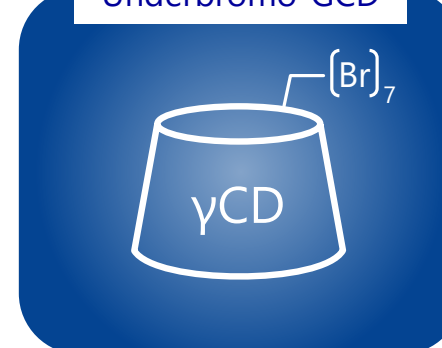
Di-Cl-Sugammadex



Mono-LAC-Sugammadex



Underbromo-GCD



For typical analysis see slide 12

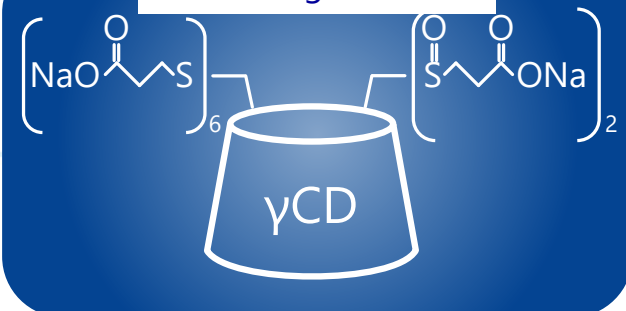
# SUGAMMADEX PROCESS IMPURITIES REGULARLY ON STOCK

Mono-SO-Sugammadex

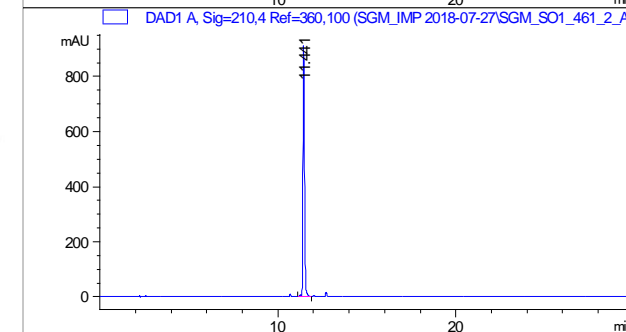
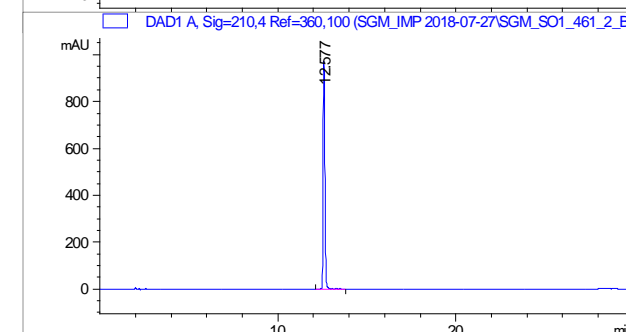
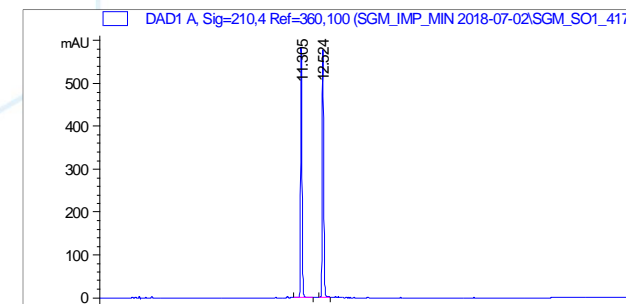


This compound is a mixture of two epimers. With our purification method these epimers were separated. The epimer mixture and the separate epimers are commercial available.

Di-SO-Sugammadex

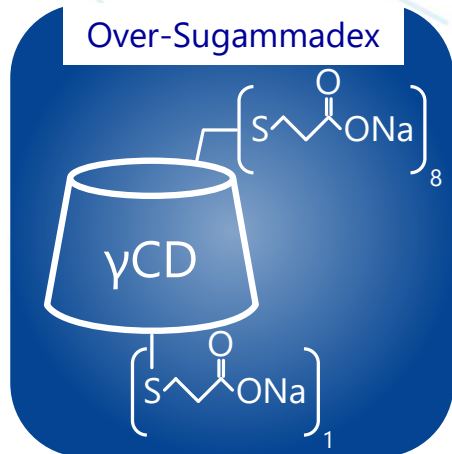


The disulfoxide derivative has also been prepared as mixture of several isomers.

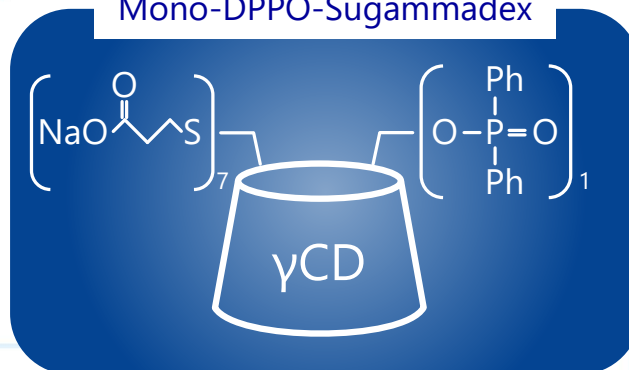


# SUGAMMADEX PROCESS IMPURITIES UNDER DEVELOPMENT

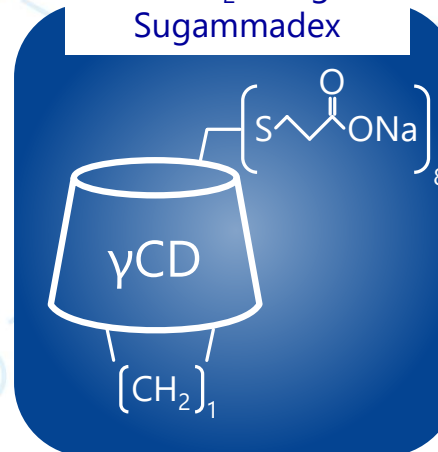
Over-Sugammadex



Mono-DPPO-Sugammadex



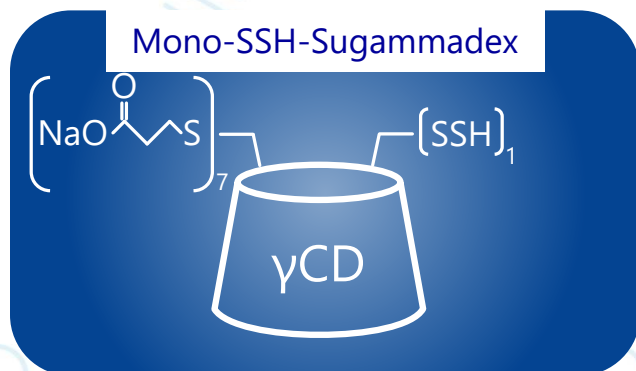
Over-CH<sub>2</sub>-bridged-Sugammadex



Underchloro-GCD

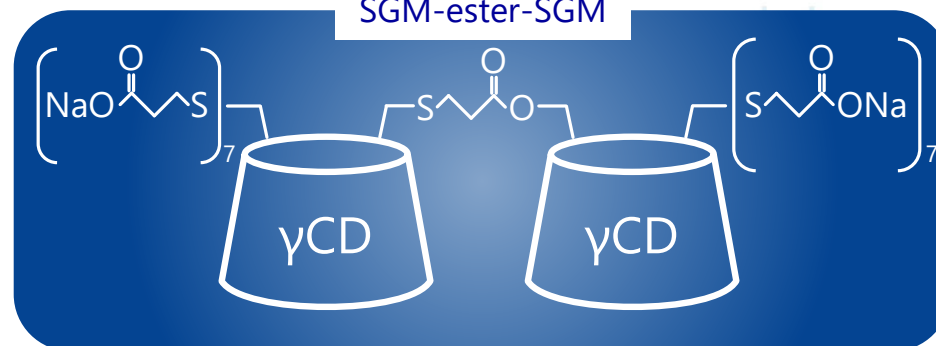


Mono-SSH-Sugammadex

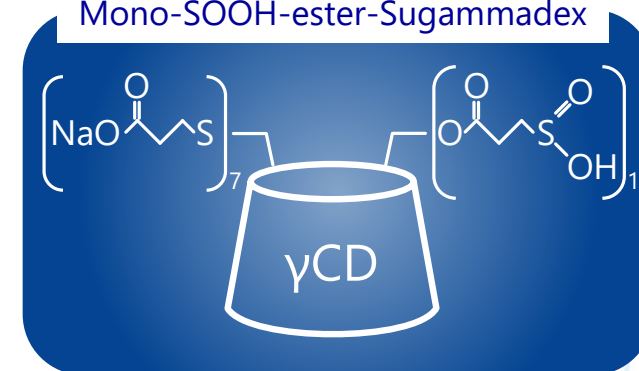


Contact us for any other  
impurities you identified in your  
generic Sugammadex!

SGM-ester-SGM



Mono-SOOH-ester-Sugammadex



# CYCLOLAB SERVICE PORTFOLIO

## RELATED SERVICES – R&D



### Early phase drug development

Customization of CD enabled formulations

Investigation of changes in physico-chemical properties

Life cycle management

### Custom cyclodextrin synthesis

Exclusive manufacture, unique synthetic routes

self-tailored products and characteristics

### In vitro bioequivalence studies

Design and performance of in vitro studies to support bioequivalence of a CD enabled formulation.

### Analytical services

Method development, validation; cGMP release testing of pharma grade CDs

HPLC, GC, CE, UV, MS, NMR, IR, Micro and BET content methods

Stability studies

CD-guest interaction studies

CD-based chiral separations

Assay, impurity tests

Bioanalytical investigations

### IP services and consultation

30 years of experience in compilation of CD related patents (synthesis, application, etc.), patent claim analysis, consultancy in CD related projects

Over 62.000 CD related papers



**SUGAMMADEX**

## **COMPANY CONTACTS**

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