CYCLOSOL® Cyclodextrins

Molecular intelligence to optimise formulation

What they are and why they matter

Unique Molecular Structure

Cyclodextrins are plant-derived (corn/potato) oligosaccharides obtained enzymatically. Their ring structure features a hydrophilic exterior and a lipophilic interior, acting as a specialised "host cavity".

This molecular architecture allows for the **inclusion of lipophilic molecules without chemically modifying them**, forming reversible inclusion complexes stabilised by Van der Waals forces.

Three Natural Types

There are three main natural cyclodextrins: **α, β and γ**, formed by 6, 7, and 8 glucose units respectively.

All are suitable for vegetarians, non-allergenic, and offer excellent safety profiles for food, pharmaceutical, and cosmetic applications.

Advantages that Create Value

For R&D, Regulatory & Marketing

Stability & Solubility

They significantly improve the stability and aqueous solubility of active compounds. They reduce volatility and **effectively mask** undesirable tastes and odours.

Ideal for sensitive actives that require protection during processing and storage.

Applications in Food & Beverages

Vegetable Emulsions

Plant-based alternative for stabilising **O/W emulsions**. Functions as a whipping aid for liquid or powdered proteins.

Innovative Mousses

Enables the creation of **mousses without fat or dairy protein**, opening up new opportunities for clean-label products.

Flavour Protection

Useful for **stabilising flavours**, **masking bitterness** and **increasing the bioavailability** of functional active ingredients.

EU-Recognised Health Claim

α-cyclodextrin: Has an officially recognised health benefit by the European Union related to the reduction of blood glucose increase after starch-rich meals.

Scientific Endorsement

This recognition is based on rigorous clinical studies that demonstrate α-cyclodextrin's ability to modulate postprandial glycaemic response.

Subject to specific conditions of use and labelling in accordance with applicable European regulations.

Commercial Opportunity

Represents a significant competitive advantage for products aimed at glycaemic control and functional nutrition.

Allows for the development of health claims supported by the European regulatory authority.

Pharmaceutical & Consumer Care

Profile Optimisation

Significantly improves the **flavour and odour** profiles of APIs, eliminating unpleasant notes that affect patient compliance.

Advanced Vehiculation

Facilitates the **efficient vehiculation** of APIs and cosmetic ingredients, significantly enhancing their performance in aqueous formulations.

Bioprocesses & Materials

Optimised Fermentation

In **fermentation** processes, cyclodextrins enable the selective extraction of lipophilic products, improving process efficiency and the purity of the final product.

Rheological Control

In polymers and paints, they act as auxiliaries for **rheological control** and as processing aids, optimising the physical properties of the final material.

Sectors We Serve

Food

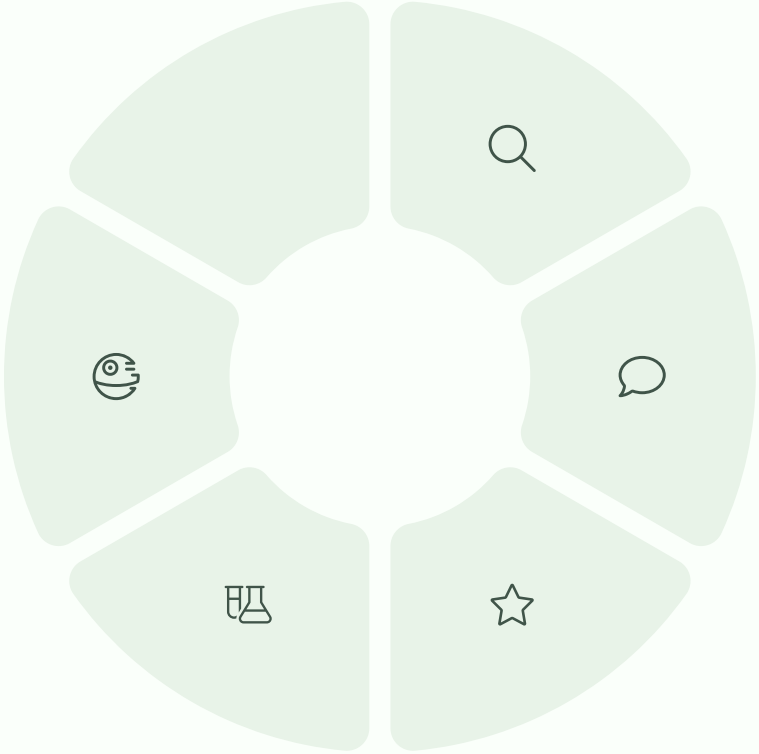
Food products and nutritional supplements with enhanced functionality

Construction

Paints and coatings with improved properties

Chemical

Process auxiliaries and property control



Personal Care

Cosmetics and hygiene products with improved stability and efficacy

Pharmaceutical

APIs and excipients for innovative formulations (R&D&I only)

Biotechnology

Fermentation and selective extraction processes

We offer **global supply** and strategic international alliances to ensure efficient and reliable service in all markets.

Why CYCLOSOL®

ND Pharma & Biotech - Your Strategic Partner

01

Comprehensive Range and Specialised Grades

We offer pharmaceutical grade (**CYCLOSOL® Pharma**), food grade (**CYCLOSOL® Food**), and standard technical grade, each with specifications adapted to its specific application.

02

Extensive Molecule Portfolio

A wide range of base molecules and functional derivatives to precisely adjust performance, flavour, solubility, and cost for each specific project.

03

Comprehensive 360° Support

Specialised technical-scientific and legal team that provides support from the initial design of the inclusion complex to the final quality dossier and labelling compliance.

CYCLOSOL® Portfolio

Selection of Main Products

α-Cyclodextrin

- **CYCLOSOL A®** - Standard Grade
- **CYCLOSOL AH®** - Hydrate Version
- **CYCLOSOL A (FG)®** - Food Grade
- **CYCLOSOL A Glucosyl®** - Glucosylated Derivative
- **CYCLOSOL ANASH®** - Sodium Sulphate Hydrate

β-Cyclodextrin

- **CYCLOSOL B®** - Standard Grade
- **CYCLOSOL B-H2O®** - Hydrate Version
- **CYCLOSOL B-MET®** - 2,6-di-O-methyl
- **CYCLOSOL B-TRIAC®** - Triacetyl Derivative
- **CYCLOSOL B-HPL®** - Hydroxypropyl Functional

γ-Cyclodextrin

- **CYCLOSOL G-PURE®** - Purity ⩾98%

Ideal for larger molecules that require wider cavities for the formation of stable complexes.

Use Cases: Functional Beverages

Flavour Optimisation

Cyclodextrins are particularly effective at **masking bitter notes** typical of plant extracts and bioactive compounds, significantly improving the palatability of the final product.

Aroma Stabilisation

They protect and **stabilise sensitive citrus aromas**, maintaining the desired organoleptic profile throughout the product's shelf life.

Improved Bioavailability

They increase the **bioavailability of plant extracts** and functional compounds, maximising the benefit for the end consumer.

Use Cases: Dairy & Plant-Based

Clean Foams

They allow for the creation of "cleaner" products with simpler, more natural labels, responding to consumer demand for recognisable ingredients.

Innovative Mousses

They facilitate the development of **mousses without added fat**, opening up new possibilities for lower-calorie and healthier products.

Superior Stability

They provide **better stability** for foams and textures, maintaining the desired properties during storage and transport.

Use Cases: Capsules and Syrups (Supplements)

1 Reduction of Unpleasant Odour/Taste

They effectively eliminate unpleasant odours and tastes from APIs, significantly improving the patient experience and increasing treatment adherence.

2 Increased Solubility

They dramatically improve the aqueous solubility of lipophilic compounds, facilitating formulation and enhancing the bioavailability of the active pharmaceutical ingredient.

3 Improved Stability

They protect sensitive APIs from degradation, extending the product's shelf life and maintaining therapeutic potency over time.

Use Cases: Fermentation & Extracts

Selective Extraction

Cyclodextrins enable the **selective extraction of lipophilic metabolites** during fermentation processes, improving product recovery efficiency.

This selectivity reduces the need for additional purification steps, simplifying the overall process and reducing operational costs.

Cleaner Processes

By facilitating the separation of compounds of interest, they contribute to developing **cleaner and more sustainable processes** in the biotechnology industry.

They reduce the use of organic solvents and minimise waste generation, aligning with green chemistry principles.

Use Cases: Paints & Polymers

1

Rheological Control

They act as specialised additives for the precise control of rheological properties, optimising applicability and flow characteristics.

2

Polymerisation Aids

They function as effective auxiliaries in polymerisation processes, improving the uniformity and final properties of the polymeric material.

3

Improved Properties

They contribute to enhancing specific characteristics such as adherence, durability, and resistance to adverse environmental factors.

Quality, Compliance and Claim Management

Specialised Grades and Documentation

We provide detailed technical datasheets, rigorous purity specifications, and comprehensive regulatory support aligned with the specific intended use.

Each grade (food, pharma, technical) features specific documentation that facilitates regulatory approval and compliance.

Responsible Claim Management

We manage the **responsible use** of available scientific evidence for α-CD in the EU, ensuring appropriate conditions of use.

We ensure labelling compliant with applicable regulations in each specific market, thereby minimising regulatory risks for our clients.

How We Work With You

Formulation Diagnosis

Detailed analysis of requirements and selection of the most suitable cyclodextrin or derivative for your specific application.

Complex Design

Optimised design of the inclusion complex and execution of exhaustive performance tests to validate effectiveness.

Scale-up and Supply

Efficient process scale-up and reliable supply in the required grade (Food/Pharma/Technical) with complete traceability.

Dossier & Compliance

Comprehensive technical-legal support to accelerate internal approvals and the development of scientifically-backed claims.

Regulatory Framework: Scope and Product

This regulatory analysis comprehensively covers α-, β-, and γ-cyclodextrin as food ingredients, including their status as additives and novel foods in the EU, GRAS classification in the USA, and requirements for cosmetics and pharmaceutical excipients.

Comprehensive Coverage

The report addresses the use of authorised health claims in the EU, specific labelling requirements, and regulatory considerations for cosmetic and pharmaceutical applications.

All references are strictly based on official legal texts and scientific opinions from competent authorities.

Scientific Approach

No claims not supported by official regulations are included. Each cited provision refers directly to current legal texts or scientific opinions from EFSA and FDA.

It provides the solid foundation necessary for responsible product development and commercial strategies.

EU: β-Cyclodextrin as an Additive (E 459)

Authorisation and Conditions of Use

Tablets and Coated Tablets

Permitted *quantum satis* in foodstuffs in the form of tablets and coated tablets, with specific exclusions according to Annex II of Regulation 1333/2008.

Powdered Beverages

Authorised up to **500 mg/kg** in flavoured powdered instant beverages (category 14.1.4).

Nutrient Preparations

Permitted up to **100,000 mg/kg** in the preparation and **1,000 mg/kg** in the final foodstuff according to Annex III, Part 4.

Purity specifications are defined in Regulation (EU) 231/2012, entry E 459. EFSA maintains the ADI of 0–5 mg/kg body weight/day previously established by the SCF.

EU: α- and γ-Cyclodextrin as Novel Foods

Regulatory Framework

Regulated under Regulation (EU) 2015/2283 (novel foods) and Implementing Regulation (EU) 2017/2470, which establishes the Union list with specific conditions of use.

α-Cyclodextrin

Included as an authorised novel food in the official Union list, with specific conditions of use and clearly defined technical specifications.

γ-Cyclodextrin

Initially authorised by Decision 2012/288/EU under the previous framework 258/97, subsequently consolidated into the Union list of 2017/2470.

For specific uses and levels of α-/γ-cyclodextrin, reference should be made to tables 1 and 2 of the Annex to Regulation 2017/2470 in its consolidated version in force.

EU: Authorised Health Claims

> "The consumption of α-cyclodextrin as part of a starch-containing meal contributes to the reduction of the blood glucose increase after that meal."

1

Specific Conditions of Use

The portion must provide ⩾ **5 g of α-cyclodextrin for every 50 g of starch** present in the meal to be able to use the authorised claim.

2

Consumer Information

It must be clearly stated that **the beneficial effect is obtained by consuming α-cyclodextrin as part of the starch-containing meal**.

3

Scientific Basis

The claim is supported by the EFSA Opinion of 2012 and is included in Regulation (EU) 432/2012 on authorised claims.

EU: Labelling and Exemptions

General Framework

Regulated by Regulation (EU) 1169/2011 on the provision of food information to consumers. Substances used as processing aids do not require declaration if they do not exert a technological effect in the final product.

A similar exemption applies to 'carry-over' additives without a technological function in the final food.

Additives Labelling

For B2B and consumer sales, see Chapter IV of Regulation (EC) 1333/2008 (articles 21-23) which specifies mandatory designations and corresponding E-numbers.

Essential for regulatory compliance and transparency towards the end consumer.

EU: Cosmetic Applications

- **Regulatory Framework**

  Regulated by EC Regulation 1223/2009. There is no specific restriction for "CYCLODEXTRIN" in Annexes II/III regarding prohibited or restricted substances.

- **Safety Requirements**

  General safety due diligence applies, including mandatory CPSR (Cosmetic Product Safety Report) and PIF (Product Information File).

- **INCI Denomination**

  In CosIng, "CYCLODEXTRIN" is listed as an official INCI denomination with recognised functions: absorbent, chelating, among other cosmetic applications.

EU: Pharmaceutical Excipients

EMA/CHMP has published an official Q&A document specifically on cyclodextrins as excipients, which constitutes the main reference for pharmaceutical developments in the EU.

1

Routes of Administration

The official document summarises the different appropriate routes of administration and the specific safety considerations for each.

2

Safety Considerations

Includes specific warnings, such as precautions in patients with renal impairment for some derived cyclodextrins.

3

Labelling Texts

Provides proposed labelling texts and warnings that must be included according to the type of cyclodextrin used.

USA: GRAS Status

FDA GRAS Notice Inventory

GRN 155

α-cyclodextrin

FDA "no questions" for use as a fibre supplement, flavour/colour/vitamin carrier, and texture improver (except meat/poultry).

GRN 74

β-cyclodextrin

FDA "no questions" as a flavour carrier/protector in multiple categories with variable levels depending on the product.

GRN 46

γ-cyclodextrin

FDA "no questions" as a stabiliser, emulsifier, carrier, and formulation aid in specific categories.

Note: GRN 678 (α-cyclodextrin) - evaluation ceased at notifier's request, does not constitute a "no questions letter".

USA: Claims and Limitations

Absence of Specific Claim

In the USA, there is no specific health claim for α-cyclodextrin equivalent to that authorised in the EU for glycaemic control.

Any structure/function claim in foods or supplements must strictly comply with FDA regulations and be scientifically substantiated.

Compliance Requirements

Claims cannot imply diagnosis, treatment, cure, or prevention of diseases without the corresponding specific authorisation.

It is fundamental to work with regulatory experts to develop appropriate claims that comply with US legislation.

USA: Pharmaceutical Excipients

FDA Database

Cyclodextrins, including derivatives such as SBE-β-CD and HP-β-CD, are listed as inactive excipients in multiple FDA-approved medicines.

1

2

Specific Precautions

Some CD derivatives require precaution in renal insufficiency (e.g., SBE-β-CD in antivirals), a criterion aligned with scientific literature.

3

Regulatory Consistency

Safety considerations are consistent with EMA recommendations in the EU, providing regulatory harmonisation.

Practical Compliance Checklist

EU - Food

- Verify use as β-CD (E 459) vs α-/γ-CD (novel food)
- Apply Annex II/III limits (1333/2008) and specifications (231/2012)
- For glycaemic claim: only α-CD under specific conditions
- Label according to 1169/2011, evaluate exemptions for processing aids

US - Food

- Align use with applicable GRAS notification (GRN 155/74/46)
- Document cGMP compliance for each application
- Do not use EU glycaemic claim
- Adjust messaging to FDA regulations without disease claims

Cosmetics (EU)

- Comply with Regulation 1223/2009 (PIF/CPSR)
- Mandatory CPNP notification
- INCI labelling "CYCLODEXTRIN" according to CosIng
- Recognised functions: absorbent, chelating

Medicinal Products

- EU: apply EMA Q&A, include proposed warnings
- US: confirm presence in IID and permitted levels
- Consider precautions for renal insufficiency
- Document public safety references

Key Legal References

EU - Regulatory Framework

- Reg. (EC) 1333/2008: Additives (E 459 β-CD)
- Reg. (EU) 231/2012: Specifications E 459
- Reg. (EU) 2015/2283: Novel foods
- Exec. Reg. (EU) 2017/2470: α/γ-CD List
- Reg. (EU) 432/2012: Health claims
- Reg. (EU) 1169/2011: Food labelling

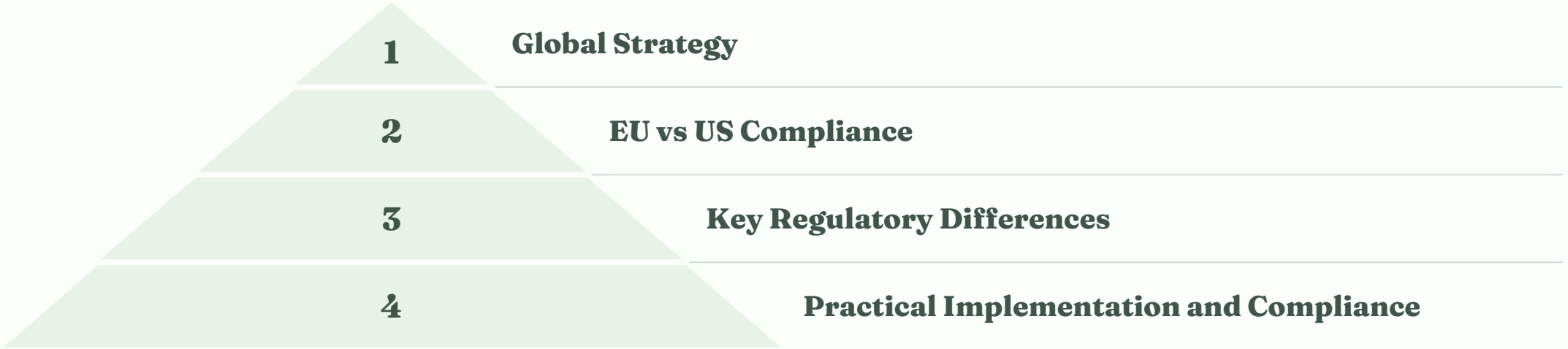
EU - Specific Sectors

- Reg. (EC) 1223/2009: Cosmetics
- CosIng: INCI Functions "CYCLODEXTRIN"
- EMA/CHMP/495747/2013: Excipients Q&A
- Decision 2012/288/EU: Historical γ-CD
- EFSA Opinion 2012: Scientific Basis α-CD

U.S. - GRAS Framework

- GRN 155: Authorised α-CD
- GRN 74: Authorised β-CD
- GRN 46: Authorised γ-CD
- GRN 678: α-CD Evaluation Ceased
- 21 CFR Part 184: GRAS Framework
- FDA IID: Pharmaceutical Excipients

Final Remarks



EU Regulatory Landscape

In the EU, **β-CD (E 459)** is the food additive with clearly defined uses and maximum levels. α-/γ-CD are regulated as novel foods with specific conditions of use.

Only the **health claim for α-CD** regarding glycaemic response is officially authorised and must comply with strict conditions of use and labelling.

US GRAS Framework

The three main cyclodextrins (α-, β- and γ-CD) have **confirmed GRAS status** by the FDA according to the corresponding GRN notifications, each with specific categories and levels.

There is no authorisation equivalent to the European glycaemic claim, requiring differentiated commercial strategies per market.