WALOCEL™ C
USP/EP Carboxymethyl Cellulose Sodium for Pharmaceutical Applications
WALOCEL™ C is highly purified sodium carboxymethyl cellulose. With a purity of 99.5%, WALOCEL™ C meets the European Pharmacopoeia (Ph.Eur. or EP) and United States Pharmacopoeia (USP) regulatory requirements for use in pharmaceutical applications. WALOCEL™ C helps control the rheological (flow) properties of many application systems.

The low batch-to-batch variation in chemical and physical characteristics makes WALOCEL™ C an excellent excipient for the formulation of sophisticated pharmaceuticals.

- **Solid dosage forms:**
  - Capsules
  - Solid-particle powders
  - Granules and pellets
  - Tablets and coated tablets

- **Semi-solid dosage forms:**
  - Ointments
  - Creams
  - Gels
  - Pastes

- **Liquid dosage forms:**
  - Solutions
  - Suspensions
  - Emulsions
Production

WALOCEL™ C is highly purified sodium carboxymethyl cellulose (Na CMC) which is an anionic derivative of cellulose. In Na CMC the hydroxyl groups are partially or fully substituted by carboxymethyl groups.

WALOCEL™ C is produced by first transforming the raw material cellulose into the more reactive form alkali cellulose by adding caustic soda. In the subsequent etherification stage the reaction vessel is fed with chloroacetic acid. The purification stage for washing out the byproducts sodium chloride and sodium glycolate is followed by a drying and milling stage to obtain WALOCEL™ C with defined particle size, bulk density and loss on drying. The purity of the finished WALOCEL™ C is above 99.5%wt.

All WALOCEL™ C grades are produced in dedicated facilities according to the requirements of IPEC Good Manufacturing Practice. These production lines have received the ISO 9001, 14001 and FSSC 22000 certificates.
Typical Properties and Regulatory Status

Beside other test items the key parameters characterizing WALOCEL™ C are:

- Degree of substitution (DS): types 0.7 or 0.9;
- Degree of polymerization that affects the viscosity of WALOCEL™ C solutions;
- Particle size distribution.

These crucial parameters are incorporated in the nomenclature of WALOCEL™ C.

<table>
<thead>
<tr>
<th>WALOCEL™ C</th>
<th>Trade name</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,400</td>
<td>Nominal viscosity of a 2% by weight solution (mPas)</td>
</tr>
<tr>
<td>GA</td>
<td>G = granule, P = powder, A = high purity</td>
</tr>
<tr>
<td>07</td>
<td>Substitution type</td>
</tr>
</tbody>
</table>

Examples

- WALOCEL™ C 30 GA → Granule, nominal viscosity of 30 mPas (2% b. weight solution), substitution type 0.9;
- WALOCEL™ C 2,400 PA 07 → Powder, viscosity of 2,400 mPas (2% b. weight solution), substitution type 0.7.

As a well-known and established excipient, sodium carboxymethyl cellulose is widely used in oral and topical formulations. It is a Generally Recognized As Safe (GRAS) listed substance and an authorized food additive. The FDA Inactive Ingredients Guide lists this excipient for, oral capsules, tablets, liquid and semi-solid products.

The compendial monographs of the EP and USP distinguish between different types: Low-substituted Carmellose sodium has a sodium content of 2.0 – 4.5 wt.-% (USP and EP) based on dried substance. Carmellose sodium has a sodium content of 6.5 – 10.8 wt.-% (EP) or 6.5 – 9.5 wt.-% (USP) based on dried substance. Carboxymethyl cellulose 12 in accordance with USP has sodium content of not less than 10.4 and not more than 12 wt.-% calculated on dry substance basis.

All WALOCEL™ C grades comply with the Carmellose sodium monographs of the USP and EP. The WALOCEL™ C product line meets the requirements of the Code of Federal Regulations of the Food and Drug Administration (FDA) Part 21 CFR 182.1745 (GRAS) Kosher and Halal certificates are available. Providing the formulator with a large number of formulation options, Dow offers several viscosity and powder types.

Additionally, within the USP/EP-compliant sodium content specification there are two different types available with regard to the degree of substitution (DS): type 0.7 and 0.9. The DS is defined as the number of carboxymethyl groups attached on average to one anhydroglucose unit of the polymeric backbone.
## Typical Properties for CMC Pharma Line

<table>
<thead>
<tr>
<th>Property</th>
<th>Unit</th>
<th>Method</th>
<th>WALOCEL™ 30 GA / WALOCEL™ 30 PA</th>
<th>WALOCEL™ 700 GA / WALOCEL™ 700 PA</th>
<th>WALOCEL™ 2400 GA / WALOCEL™ 2400 PA / WALOCEL™ 2400 GA 07</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium Content (Assay)</td>
<td>%</td>
<td>USP/EP</td>
<td>6.5 - 9.5</td>
<td>6.5 - 9.5</td>
<td>6.5 - 9.5</td>
</tr>
<tr>
<td>DS Type</td>
<td></td>
<td></td>
<td>0.9</td>
<td>0.9</td>
<td>0.9 / 0.7</td>
</tr>
<tr>
<td>Identification A, B, C (USP)</td>
<td></td>
<td>USP</td>
<td>pass</td>
<td>pass</td>
<td>pass</td>
</tr>
<tr>
<td>Identification A, B, C (EP)</td>
<td></td>
<td>EP</td>
<td>pass</td>
<td>pass</td>
<td>pass</td>
</tr>
<tr>
<td>Heavy Metals</td>
<td>ppm</td>
<td>USP/EP</td>
<td>&lt; 20</td>
<td>&lt; 20</td>
<td>&lt; 20</td>
</tr>
<tr>
<td>Viscosity (Brookfield 2 % / 25° C)</td>
<td>mPas</td>
<td>USP</td>
<td>25 – 36 (Spindle 1 / 60 RPM)</td>
<td>560 – 840 (Spindle 2 / 30 RPM)</td>
<td>1920 – 2880 (Spindle 3 / 30 RPM)</td>
</tr>
<tr>
<td>Viscosity (Rotovisko 2 % / 20° C / D = 10 s⁻¹)</td>
<td>mPas</td>
<td>EP</td>
<td>23 - 42</td>
<td>525 - 980</td>
<td>1800 - 3360</td>
</tr>
<tr>
<td>pH</td>
<td></td>
<td>USP/EP</td>
<td>6.5 - 8.0</td>
<td>6.5 - 8.0</td>
<td>6.5 - 8.0</td>
</tr>
<tr>
<td>Loss on Drying</td>
<td>%</td>
<td>USP/EP</td>
<td>&lt; 10</td>
<td>&lt; 10</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Appearance of Solution / Opalescence</td>
<td></td>
<td>EP</td>
<td>pass</td>
<td>pass</td>
<td>pass</td>
</tr>
<tr>
<td>Sodium glycolate</td>
<td>%</td>
<td>EP</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>Chlorides</td>
<td>%</td>
<td>EP</td>
<td>&lt; 0.25</td>
<td>&lt; 0.25</td>
<td>&lt; 0.25</td>
</tr>
<tr>
<td>Sulfated ash</td>
<td>%</td>
<td>EP</td>
<td>20.0 - 33.3</td>
<td>20.0 - 33.3</td>
<td>20.0 - 33.3</td>
</tr>
<tr>
<td>Residual Solvents</td>
<td></td>
<td>USP/EP</td>
<td>Pass</td>
<td>Pass</td>
<td>Pass</td>
</tr>
</tbody>
</table>

1 These are typical properties, not to be construed as specifications
Properties

- WALOCEL™ C is a white to slightly off white powder with a high chemical and microbiological purity and stability. This vegetable excipient is practically free of odor and taste. WALOCEL™ C is compatible with most of the common active ingredients and excipients. However, as an anionic polymer it may form complexes with gelatin and pectin.

- WALOCEL™ C is insoluble in most organic solvents such as ethanol, methanol or acetone. WALOCEL™ C can be dissolved in mixtures if the content organic solvent is less than 40 percent by weight.

- WALOCEL™ C is highly soluble in water at all temperatures offering clear solutions and various viscosities depending on the selected WALOCEL™ C grade and its concentration (see Figure 1). The measuring conditions including shear rate and temperature also influence the viscosity considerably (see Figure 2). An increase in temperature or shear rate will reduce the viscosity. This effect is completely reversible: after cooling the solution or reducing the shear rate, the viscosity returns to its initial value.

- Aqueous solutions of WALOCEL™ C are stable over a broad pH range but free CMC acid may precipitate below pH 2 – 3. The pH limit for precipitation depends on the molecular weight and degree of substitution: a lower molecular weight and higher degree of substitution tend to lower the pH of precipitation.

- Univalent metal ions slightly reduce the viscosity of aqueous solutions of WALOCEL™ C but polyvalent cations may cause flocculation. Resistance to salts depends on the degree of substitution: the higher the DS, the more stable the viscosity. The precipitates are generally white to colorless with the exception of iron, copper or chromium salts and can be dissolved in sodium hydroxide solutions.

- WALOCEL™ C does not reduce the surface tension of water. Typical values for WALOCEL™ C solutions are in the range of 71 mN/m. The surface tension of water is 72 mN/m. WALOCEL™ C increases the freeze/thaw stability of water based formulations by reducing the water loss during freeze/thaw cycles.

- WALOCEL™ C has an excellent water binding capacity. The amount of water absorbed depends on the viscosity and substitution type of the selected WALOCEL™ C grade as well as on the temperature. The lower the degree of substitution and the higher the viscosity, the higher the water absorption capacity of WALOCEL™ C will be.

- WALOCEL™ C solutions offer crystal clear films which are resistant to oil, fat and organic solvents. These films can be plasticized with e.g. glycerol or sorbitol.
Uses – A Real Versatile Excipient

WALOCEL™ C is a versatile excipient for e.g. oral and topical applications. Whenever viscosity control, water absorption or water retention is required, WALOCEL™ C is an excellent choice. Its tailored pseudoplastic flow behavior makes WALOCEL™ C to an enhanced suspension stabilizer.

• The low-viscosity WALOCEL™ C 30 GA and 30 PA and grades offer highly transparent solutions that are almost free of fibers. Therefore, these grades can be used for tablet coatings.

• Creams and ointments can be formulated by using the medium-viscosity grades WALOCEL™ C 700 and C 2,400 to control the rheology.

• Due to its high water absorption capacity WALOCEL™ C 2,400 is an excellent ingredient in wound care and self-adhesive ostomy products.

• The adjustable, pseudoplastic flow behavior of WALOCEL™ C facilitates tailored stabilization of suspensions. For instance in antacid formulations, WALOCEL™ C 2,400 can be used at addition rates of 0.1 – 0.3 percent by weight.

• Restrictions: use of WALOCEL™ C in injectable and parenteral applications is not supported.

Handling, Packaging and Storage

A materials safety data sheet is obtainable from Dow Pharma & Food Solutions and should be requested before handling WALOCEL™ C.

WALOCEL™ C is a stable but hygroscopic material. Therefore it should be stored in closed containers. WALOCEL™ C is packaged in 25 kg bags and delivered on shrink-wrapped, non-returnable pallets (net weight 1,000 kg).

There are no restrictive regulatory requirements regarding storage. The product should be stored in its original package in a clean and dry place, away from any sources of heat.

A re-evaluation period of 540 days is specified for WALOCEL™ C stored under the recommended conditions.

Disposal Considerations
Dispose in accordance with all local, state (provincial) and federal regulations. Empty containers may contain hazardous residues. This material and its container must be disposed in a safe and legal manner.

It is the user’s responsibility to verify that treatment and disposal procedures comply with local, state (provincial) and federal regulations. Contact your Dow Technical Representative for more information.

Product Stewardship
Dow has a fundamental concern for all who make, distribute, and use its products, and for the environment in which we live. This concern is the basis for our product stewardship philosophy by which we assess the safety, health, and environmental information on our products and then take appropriate steps to protect employee and public health and our environment. The success of our product stewardship program rests with each and every individual involved with Dow products - from the initial concept and research, to manufacture, use, sale, disposal, and recycle of each product.

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