

PHARMA-GRADE SUSPENSION AIDS FOR YOUR PERFECT MIX

Looking for more than the status quo? Or patient-friendly formulations that support high adherence to therapy? Or a cost-friendly suspension that consistently and effectively delivers active ingredients without a second thought to stability? Our broad, unique product portfolio and deep application expertise provide the versatile and reliable performance you crave, with stand-alone and synergistic solutions to help perfect your mix. Our decades of experience working alongside pharmaceutical customers, coupled with our problem-solving and staunch commitment to quality means we can design the optimal suspension formulation to help you succeed.

Suspension Aids with Functionality and Flow

Pharmaceutical liquids can improve patient compliance for pediatrics, geriatrics, and patients who have difficulty swallowing. Table 1 lists the various categories of ingredients that brand owners and formulators consider when designing for effective oral liquid pharmaceutical delivery.

IFF suspending agents, protective colloids and viscosifiers can help liquid formulations outperform the competition – allowing formulators to not only formulate stable pharmaceutical liquids but also dial in the desired viscosity,

pourability and mouthfeel. We want to introduce you to three families of our pharmaceutical excipients and how they can help reach your objectives: Avicel® colloidal microcrystalline cellulose (cMCC), GRINDSTED® Xanthan PRM and TEXTURECEL™ carboxymethylcellulose sodium (NaCMC). Product grades for each are listed in Table 2.

Table 1: Categories of Suspension Ingredients.

Categories of Suspension Ingredients	
• Drug	• Preservative
• Suspending agent (or flocculant)	• Buffer
• Dispersant (for hydrophobic drug)	• Sequestrant
• Protective colloid	• Flavor
• Sweetener	• Color
• Viscosifier	• Water

*Categories in bold indicate where IFF’s extensive excipient portfolio can help deliver the desired functionality.

Table 2: Top IFF product grades for suspension excipients.

Avicel® cMCC	GRINDSTED® Xanthan PRM	TEXTURECEL™ NaCMC
Avicel® RC-591 Avicel® CL-611	GRINDSTED® Xanthan Clear 80 PRM GRINDSTED® Xanthan 80 PRM Plus GRINDSTED® Xanthan 200 PRM Plus GRINDSTED® Xanthan Easy PRM	TEXTURECEL™ 1,000 PA 07 & GA 07 TEXTURECEL™ 2,000 PA 07 & GA 07 TEXTURECEL™ 4,000 PA 07 & GA 07 TEXTURECEL™ 20,000 PA 07 & GA 07 TEXTURECEL™ PRM 2400 GA 07

OUR FAMILY OF PHARMA EXCIPIENTS

Avicel® cMCC – A first choice suspending agent

Pharmaceutical grade Avicel® cMCC products are the industry-leading colloidal microcrystalline cellulose on the market. Why? Because gram for gram, they deliver the functionality that customers desire. Avicel® RC-591 and CL-611 are co-processed excipients

containing both MCC and NaCMC as shown in Figure 1.

Avicel® RC-591 is designed for high-shear applications, while Avicel® CL-611 is the best choice for low-shear applications. Typical use levels and product applications

are shown in Table 3. Table 4 shows the morphology of these products along with application compliance and certification information.

Figure 1: Chemical structure of Avicel® cMCC pharmaceutical grades.

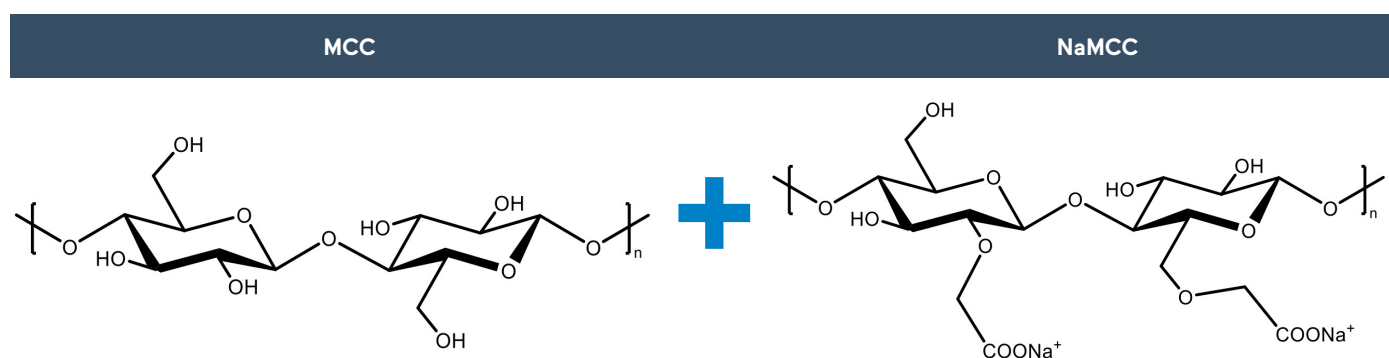


Table 3: Typical applications for pharmaceutical grade Avicel® cMCC

Product	NaCMC content (%)	Viscosity (cps)	Recommended use levels	Product Applications
Avicel® RC-591 NF	8.3-13.8	39-91 (1.2% Solids)	1.2-1.5%	<ul style="list-style-type: none"> • Oral suspensions • Nasal sprays • Topical sprays and lotions
Avicel® CL-611 NF	11.3-18.8	50-118 (2.6% Solids)	2.4-2.6%	<ul style="list-style-type: none"> • Oral suspensions • Nasal sprays • Reconstitutable suspensions • (use level ≥ 4%)

Table 4: Morphology and Certifications for Avicel® cMCC pharmaceutical grades.

Morphology	Compliance & Certifications
	<ul style="list-style-type: none"> • NF, Ph Eur., BP, JPE Compliant • Kosher and Halal Certified • Manufactured under GMP conditions with non-genetically modified organisms (non-GMO) raw materials

Dispersing and activating Avicel® cMCC for functionality

Avicel® cMCC suspending aids demonstrate thixotropic properties, forming gel-like structures at rest and exhibiting shear thinning during shaking and handling. Figure 2 shows the shear thinning that occurs at various shear rates and levels of Avicel® RC-591 in deionized water. Figure 3 shows a schematic to portray the recovery of viscosity and gel-like structure after shaking and handling. This thixotropic behavior profile allows viscous formulations to be thinned for easy swallowing with the shake of a bottle,

consistently keeping the desirable mouthfeel until the liquid is poured and swallowed. The gel-like structure recovers with time, ensuring formulation stability and content uniformity during storage.

Activating the gel-like structure is vital to achieving the desired suspension performance. With options for both high- and low-shear dispersion processes, it is no wonder Avicel® cMCC is the industry-leading colloidal MCC for diverse applications.

Avicel® CL-611 can be used where low shear is preferred, enabling the gel-like structure to build and activate in both liquid and reconstitutable suspensions. For liquid formulations, recommended use level starts at ~2.4 percent. For dispersion of dry powders that will be mixed into water, levels of 4 percent or more are recommended to achieve the desired functionality.

Figure 2: Thixotropic characteristics of Avicel® RC-591.

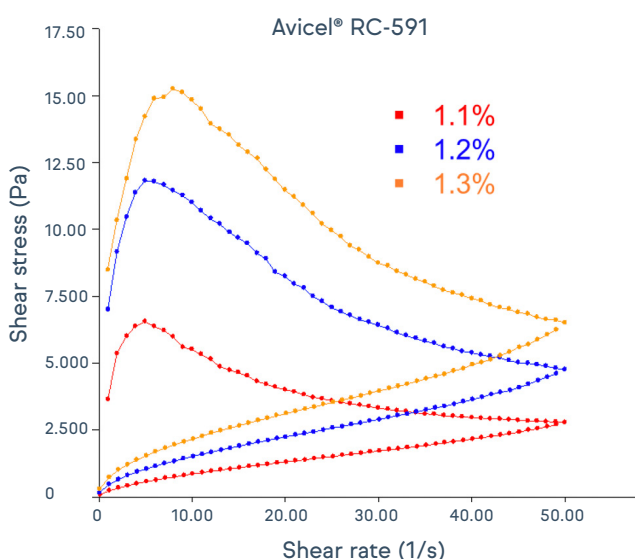
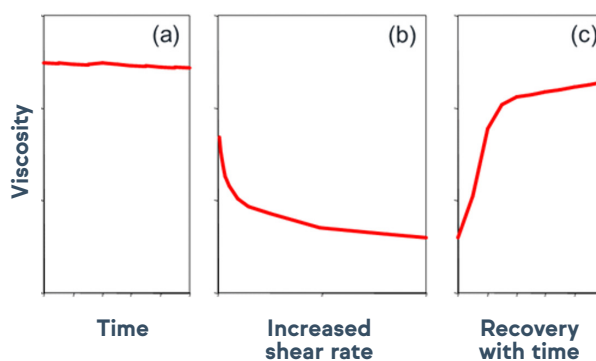


Figure 3: Avicel® RC-591 viscosity consistency at rest (a), during shaking and handling (b), and recovery post handling (c).



GRINDSTED® Xanthan PRM – Robust Thickener for Extremes

GRINDSTED® Xanthan Gum is one of the most robust and efficient excipients, tolerating high salt content, high temperature and is stable in a wide pH range. It readily dissolves in water under ambient conditions without the need of special high-shear equipment. Low levels of GRINDSTED® Xanthan PRM products can provide desirable viscosities and textures. At the same time, their pronounced shear-thinning behavior makes handling of even highly viscous solutions manageable.

Xanthan is a polysaccharide with a cellulosic backbone and trisaccharide side chains on every other -1,4-linked glucose unit, as shown in Figure 4. With a range of different morphologies and particle size distributions, GRINDSTED® Xanthan PRM pharmaceutical grades provide options for the most demanding excipient applications, as shown in Table 5.

Figure 4: Chemical Structure of GRINDSTED® Xanthan PRM pharmaceutical grades.

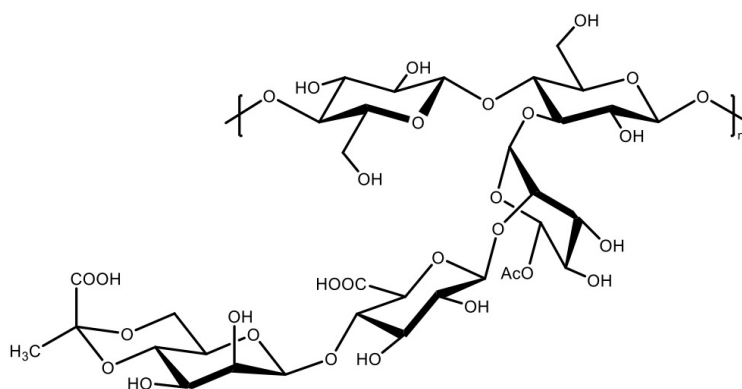


Table 5: Grades, particle size and applications for GRINDSTED® Xanthan PRM pharmaceutical excipients.

Grades	Sieve (%)	Clarity (cps)	Application use levels
GRINDSTED® Xanthan 200 PRM Plus	200 mesh Fine powder	Turbid	Fast hydration and swelling, low dispersibility – suitable in low available water medium
GRINDSTED® Xanthan 80 PRM Plus	80 mesh Coarse Powder	Turbid	Suspension stabilizer, thickener, improved texture and sensory properties
GRINDSTED® Xanthan Clear 80 PRM	80 mesh Coarse Powder	Translucent	Transparent solutions, thickener, improved texture, and sensory properties
GRINDSTED® Xanthan Easy PRM	20 mesh Granulate	Turbid	Improved flow behavior of the solid, good dispersion in water with slow hydration

Compliant & Certified for Diverse Applications

Application possibilities are endless, and we are committed to helping you be successful. That's why we have GRINDSTED® Xanthan PRM grades that are:

- US and European Pharmacopoeia compliant
- Kosher and Halal certified
- Developed by traditional non-GMO technique under GMP conditions

Unique and Complementary Strengths
Xanthan quickly hydrates and dissolves at ambient temperatures. No special high-shear equipment is required. As a rule of thumb, hydration takes 15-30 minutes with a good high-speed mixer and up to 1 hour with a slow mixer. Depending on the Xanthan product grade, solutions are translucent (clear grades) or turbid (standard grades), as mentioned in Table 5 and shown in Figure 6.

Figure 5: Morphology of GRINDSTED® Xanthan PRM pharmaceutical grades.

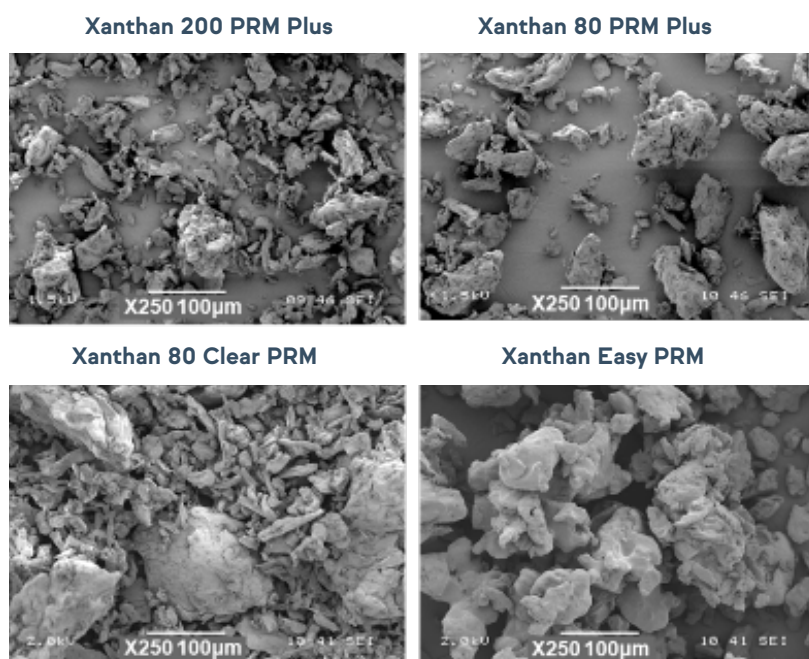
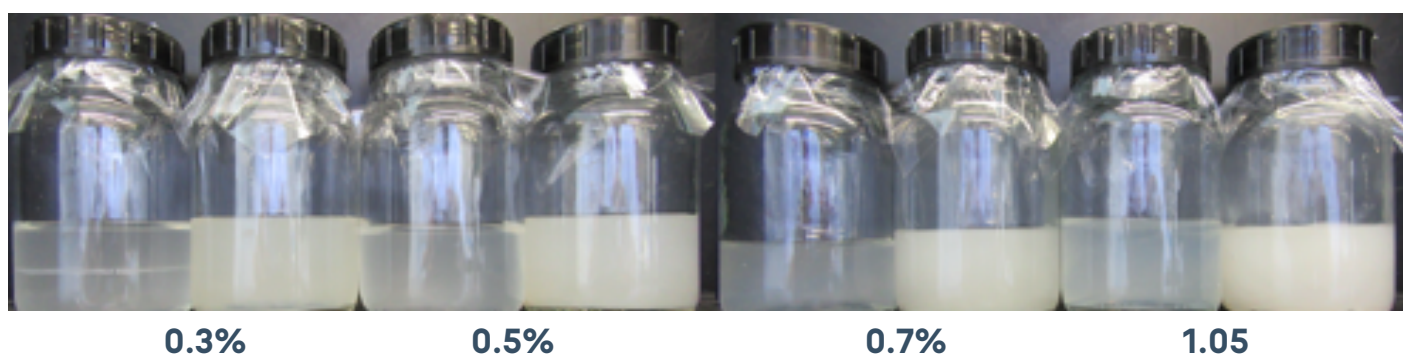


Figure 6: Appearance of solutions of GRINDSTED® Xanthan PRM Clear 80 (left) & PRM 200 (right) in DI water.



Xanthan is soluble in cold water and can create an extremely high viscosity at low concentrations. Solutions with GRINDSTED® Xanthan Gum exhibit shear thinning behavior. They have the added advantage of being heat- and pH- stable, with sustained performance in a pH window between 2 and 12. Contributing to this stability are anti-syneresis (high water-retention) properties, which also keep Xanthan highly functional in solutions with high concentrations of various salts. The

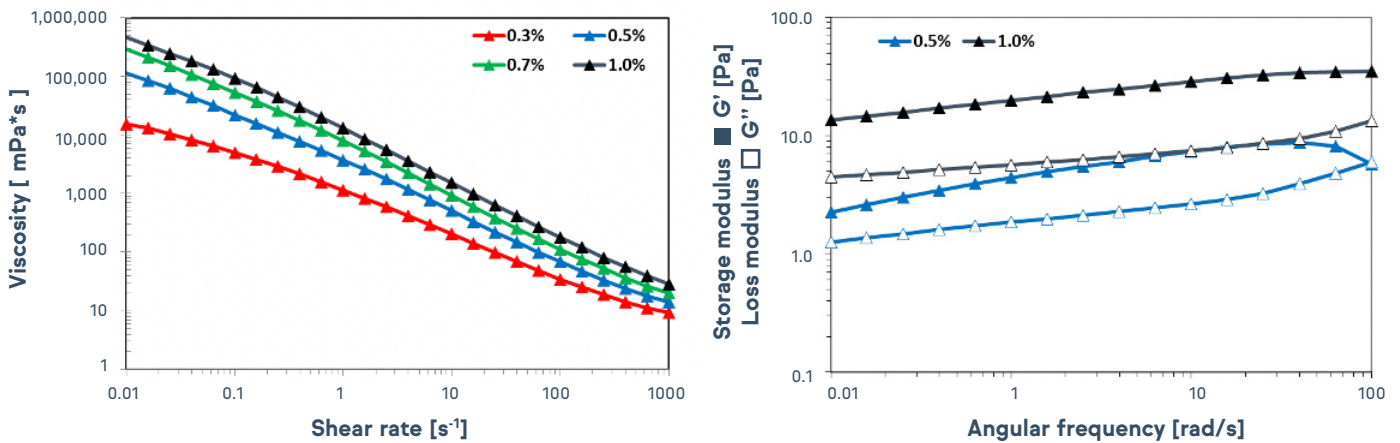
stability of GRINDSTED® Xanthan Gum and IFF's pharmaceutical product portfolio will be the subject of a future paper.

Figure 7 shows the rheological behavior of aqueous solutions containing GRINDSTED® Xanthan PRM in deionized water and the takeaways from these experimental studies.

Highly efficient GRINDSTED® Xanthan PRM products enable low use levels

(0.05-0.5 percent) in liquids. They are robust and versatile suspending agents for both liquid and powder formulations, serving as viscosifiers and thickening agents. They offer yet another option in IFF's diverse excipient portfolio, along with experienced collaborators who are ready to tackle challenging applications with you. Be sure to look for a deeper dive into the stability our important suspending aids can bring to those challenges.

Figure 7: Rheological behavior of GRINDSTED® Xanthan in deionized water.



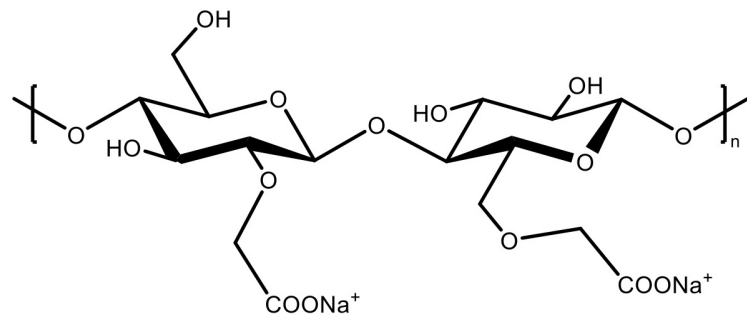
- Pseudoplasticity
- High viscosities at low use levels
- High viscosities at low shear

- Xanthan forms gel-like networks
- $G' > G''$, indicating suspending functionality in suspensions

TEXTURECEL™ NaCMC – Clearly a Versatile Viscosifier

TEXTURECEL™ NaCMC controls the rheological (flow) properties in a variety of liquid dosage forms. The chemical structure is shown in Figure 8. It is an excellent choice for viscosity control, suspension stabilization, and improved mouthfeel. TEXTURECEL™ NaCMC pharmaceutical grades are highly purified NaCMC that form clear solutions in water at all temperatures and offer a wide range of viscosities. They have no taste or odor and are compatible with most other hydrocolloids.

Figure 8: Chemical structure of TEXTURECEL™ carboxymethylcellulose sodium.



Versatility by Design

TEXTURECEL™ product lines comply with the US Pharmacopoeia and are certified Kosher and Halal. For compliance with both US and European Pharmacopoeia, we offer TEXTURECEL™ PRM grades. Most grades are non-GMO as well. The partial substitution of the hydroxyl groups with anionic carboxymethyl

groups creates a cellulose derivative with unique properties. NaCMCs serve as thickening agents, viscosifiers and suspending agents for liquid and powder formulations. Besides solutions and suspensions, they are also widely used in other semi-solid and liquid dosage forms, including ointments, creams, gels, pastes, and emulsions.

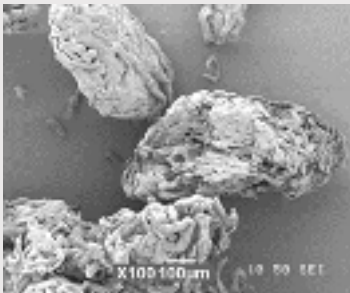
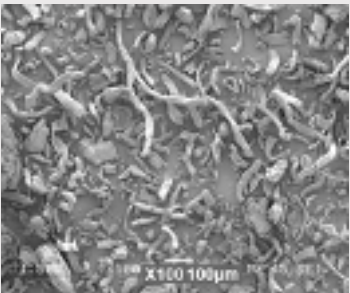
Common use levels in liquids range from 0.1-1 percent, with a variety of grades that can help dial in the desired viscosities. Table 6 shows the viscosities at 1% and 2% levels.

Table 6: Achievable viscosities at various levels of TEXTURECEL™ NaCMC in aqueous solution.

Grades	Viscosity (mPa.s)	Application
TEXTURECEL™ 1,000 PA & GA 07	300-600 (2%)	Clear solutions, viscosifier, thickener, stabilizer, binder, protective agent, improved texture and sensory properties
TEXTURECEL™ 2,000 PA & GA 07	1900-2800 (2%)	
TEXTURECEL™ 4,000 PA & GA 07	400-700 (1%)	
TEXTURECEL™ 20,000 PA & GA 07	1900-2600 (1%)	
TEXTURECEL™ PRM 2400 GA 07	1920-2880 (2%)	

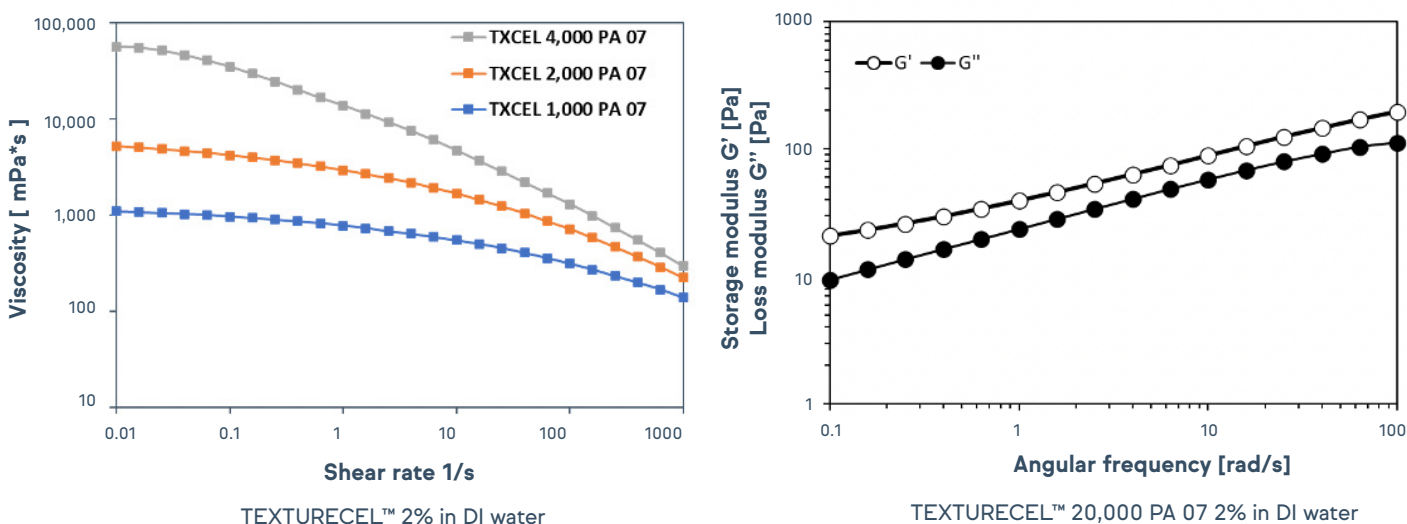
To meet the needs of your process, TEXTURECEL™ NaCMC products are offered in two particle size grades in addition to the viscosity options. Our granular (GA) and powder (PA) grades feature different particle size distributions as shown in Table 7.

Table 7: Particle size and morphologies of GA and PA grades of TEXTURECEL™ NaCMC pharma-grade products.

Sieve [mm]	Grades		Morphology	
	GA	PA	20,000 GA 07	20,000 PA 07
< 2.0	100%			
< 1.0	min. 98%			
< 0.4	max. 50%			
< 0.25		min. 93%		
< 0.16	max. 10%			
< 0.063		40-70%		

TEXTURECEL™ NaCMC also exhibits shear-thinning behavior, and the shear rate dependence increases with viscosity grade as shown in Figure 9. The gel-like networks indicate some suspending functionality in suspensions.

Figure 9: Rheological behavior of TEXTURECEL™ NaCMC at 2% in deionized water.



- Pseudoplastic, shear rate dependence increase with viscosity grade
- Forms gel-like networks, $G' > G''$, indicating suspending functionality in suspensions

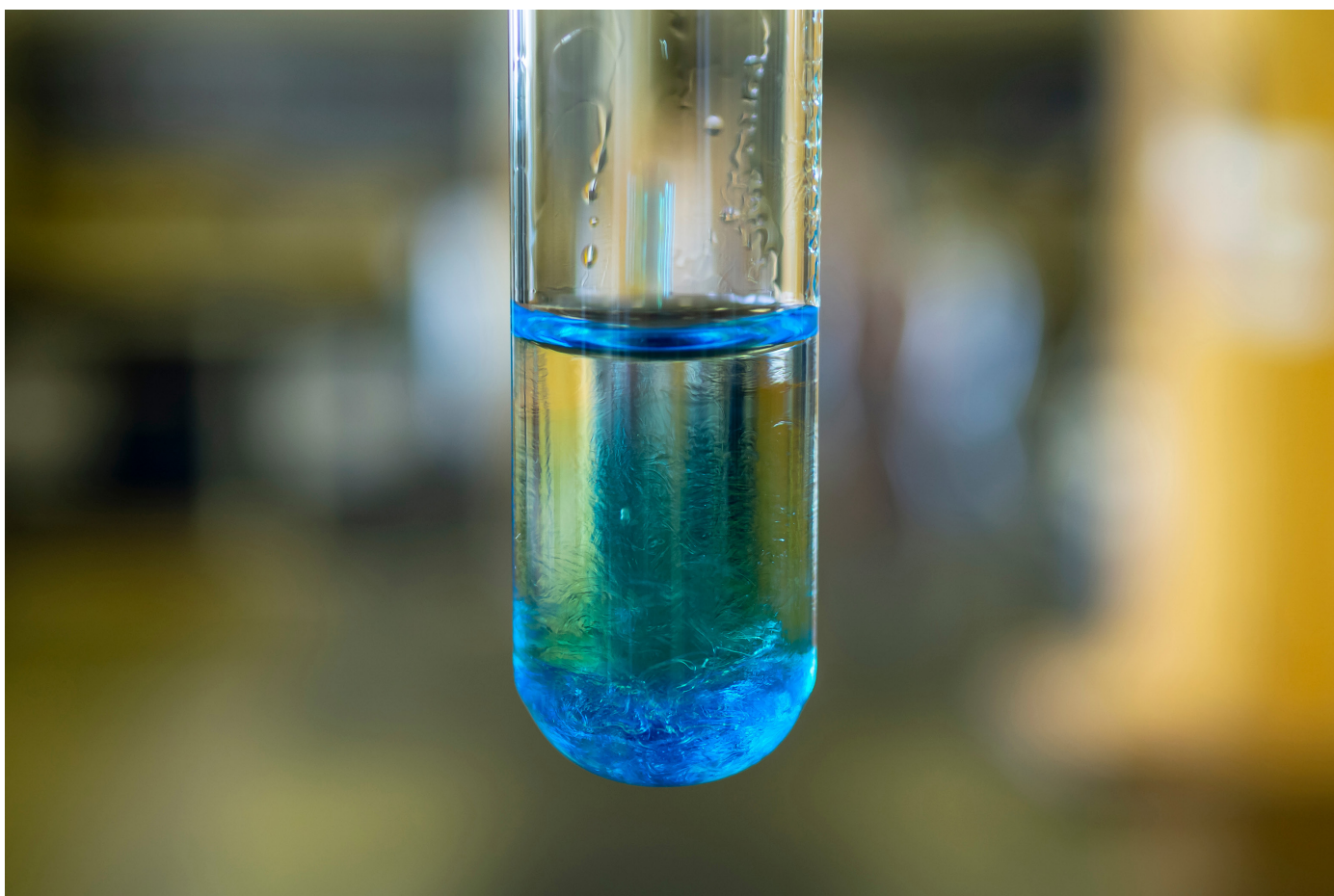
Customers choose TEXTURECEL™ NaCMC for:

- Clear and transparent solutions
- Functionality as thickener, stabilizer, binder or protective agent
- Rheology control
- Solubility in hot and cold water
- No taste or odor
- Its compatibility with other hydrocolloids

Choosing the Right Ingredients and the Right Partner

With IFF's versatile product portfolio and passion for application design, you do not have to make tough choices on your own. We can help you cut through the challenge of designing high-performance suspensions and liquid formulations with an unmatched array of leading excipients – Avicel®, GRINDSTED® and TEXTURECEL™.

Let's get started!



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& creativity meet