



CARBOPOL® POLYMERS
FORMULATION AND
PROCESSING GUIDE
FOR ORAL SOLID
DOSAGE FORMS

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Introduction

Lubrizol Life Science Health (LLS Health) specializes in pharmaceutical partnership and helping clients from idea to execution by providing best-in-class excipients for pharmaceutical prescription and over-the-counter products. When you partner with LLS Health, you benefit from working with us at every stage in the development process, with the ultimate goal of creating solutions that improve patient lives.

LLS Health is one of the world's largest manufacturer of pharmaceutical grade carbomers, polycarbophil, and thermoplastic polyurethanes and has been manufacturing pharmaceutical excipients for more than 35 years.

Our Carbopol® polymers and Noveon® polycarbophil are excipients of acrylic acid, chemically crosslinked with polyalkenyl alcohols or divinyl glycol. These polymers have been successfully formulated into a variety of different commercial oral formulations, including swallowable (peroral), chewable, buccal, and sublingual tablets.

LLS Health excipients can impart the following to an oral solid pharmaceutical product:

- **Extended release**
- **Mucoadhesion/bioadhesion**
- **Taste-masking**
- **Size reduction (of tablets)**
- **Efficient binding**

Carbopol polymers and Noveon polycarbophil offer formulation flexibility as they can be used with a variety of active pharmaceutical ingredients (APIs) and excipients, and can be processed by direct compression, dry granulation (roller compaction, slugging), or wet granulation (high/low shear, extrusion spheronization) methods. Carbopol polymers and Noveon polycarbophil provide highly effective controlled-release properties at low concentrations. Typical usage levels in extended-release tablets are 5-30%, depending on the drug properties, co-excipients, and processing parameters.

LLS Health products are supported by substantial literature references citing their performance in solid dosage forms. Additionally, Lubrizol researchers support customers in the development of new products, concepts, prototype formulations, and custom formulations through global technical service centers.



Recommended Polymers for Solid Dosage Forms

Table 1. Carbopol polymers and Noveon polycarbophil for oral solid dosage forms.

Product Trade Name	Pharmacopeia Monograph Compendial Name			Product Details			
	United States (USP/NF)	Europe (Ph. Eur.)	Japan (JPE) ¹	Polymerization Solvent	Crosslinker Type	Physical Form	Comments
Carbopol® Polymers							
71G NF	Carbomer Homopolymer Type A	Carbomers	Carboxyvinyl Polymer	Ethyl Acetate	Allyl ethers of pentaerythritol	Granular	Chemically the same as Carbopol® 971 NF polymer with no additives. Ideal for use in direct compression processes due to its improved flow properties.
971 P NF	Carbomer Homopolymer Type A	Carbomers	Carboxyvinyl Polymer	Ethyl Acetate	Allyl ethers of pentaerythritol	Powder	Lightly crosslinked polymer
974 NF	Carbomer Homopolymer Type B	Carbomers	Carboxyvinyl Polymer	Ethyl Acetate	Allyl ethers of pentaerythritol	Powder	Highly crosslinked polymer
Noveon® Polycarbophil							
AA-1 USP	Polycarbophil	–	–	Ethyl Acetate	Divinyl glycol	Powder	Ideal for mucoadhesive tablets due to its bioadhesive properties

1. Based on customer request, Lubrizol certifies select lots of product against the JPE Carboxyvinyl Polymer Monograph.

Some commercially available formulations contain Carbopol 934P NF polymer, which is polymerized in benzene. This material should not be used for new product development due to regulatory restrictions on the presence of benzene in pharmaceutical products. It may be desirable to substitute a benzene polymerized carbomer with a non-benzene polymerized carbomer in a pharmaceutical formulation. Lubrizol offers recommended substitutes for the benzene grade Carbopol products based on viscosity criteria.

Carbopol Polymers vs. Carbomers

Carbopol polymers are a product brand name of The Lubrizol Corporation. Carbopol was the first marketed carbomer and undergoes strict LLS Health testing requirements that ensure product quality and safety. In contrast, “carbomer” is a generic name that can be used to describe any high-molecular-weight polymer of acrylic acid crosslinked with allyl ethers of polyalcohols. Carbomer is also the pharmacopeial name of Carbopol polymers (see Regulatory Status of Polymers).



Regulatory Status of Polymers

Regarding compendial classification, the European Pharmacopeia has only one monograph, titled “Carbomers” which applies to Carbopol polymers. Similarly, the Japanese Pharmaceutical Excipients (JPE) also has a single monograph titled “Carboxyvinyl Polymer.”

The United States Pharmacopeia/National Formulary has several monographs for different carbomer grades. The monographs applicable for oral pharmaceutical grade products based on polymer structure, are “Carbomer Homopolymer” and “Polycarbophil” in the table above. The differentiation between Type A and B within “Carbomer Homopolymer” is based on viscosity characteristics.



Key Benefits of Lubrizol Pharmaceutical Polymers

- Highly efficient at low polymer levels (typical use levels are 5-30%), enabling smaller tablet sizes and overall formulation cost savings.
- Provide flexibility in achieving a target release profile
 - Varying the polymer level in the formulation is an effective formulation tool for controlled drug release in both monolithic and multi-particulate systems.
 - Compared to cellulosic materials, the drug release profile from a Carbopol polymer matrix can be more easily modulated by changing the polymer level.
- Can be used alone or in synergy with other Carbopol polymer grades or other commonly used controlled release excipients.
- Available in both powder and granular forms (Carbopol 71G NF) and can be used in all types of tablet manufacturing processes (wet and dry granulation, direct compression) without the addition of a tablet binder.
- Provide excellent tablet hardness and low friability over a wide range of compression forces that do not affect drug release.
- Improve the bioavailability of certain drugs.
- Impart functional attributes such as bioadhesion and taste-masking, (see **Additional Notes for Formulating with Carbopol and Noveon Polymers** section).
- Unaffected by Transmissible Spongiform Encephalopathy (TSE)/ Bovine Spongiform Encephalopathy (BSE) or Genetically Modified Organism (GMO) concerns.
- Possess global pharmacopeial status and are supported by Drug Master Files (DMFs) in the United States and Europe.
- Enable the development of patentable technologies for product differentiation and/or life-cycle extension.



Drug Release Mechanism from Tablets with Lubrizol Polymers

Carbopol polymers and Noveon polycarbophil are efficient matrix-forming excipients. These polymers are not soluble and are swellable in water. In contrast, other hydrophilic controlled-release excipients, such as hydroxypropyl methylcellulose, are linear polymers, not chemically crosslinked and, therefore, water-soluble.

The drug is dispersed homogeneously throughout the polymer matrix. Drug release from tablets and capsules with Carbopol polymers or Noveon polycarbophil is controlled by:

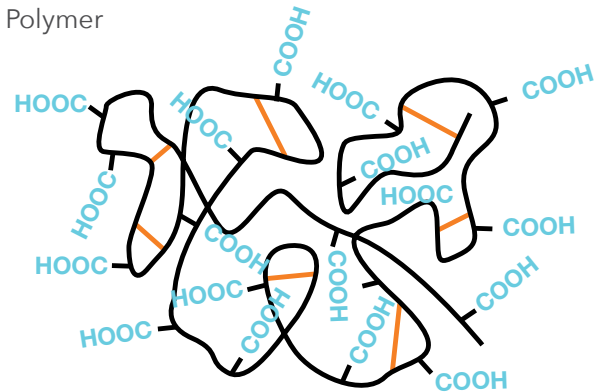
- Drug diffusion through the gel layer that the polymer forms in contact with the aqueous medium.
- Matrix (polymer) relaxation.

When carbomer tablets are placed in contact with the dissolution medium, the following occurs:

- A drug in the outside layer exposed to the bathing solution is dissolved and then diffuses out of the matrix.
- The polymer swells to form a hydrated matrix layer (hydrogel) (**Figure 1**). Due to the crosslinked nature of the polymers, the hydrogel is not comprised of single entangled chains of polymers (as is the case with linear polymers) but is comprised of discrete microgels made up of many polymer particles in which the drug is dispersed.
- The hydrated matrix layer controls water penetration (into the non-hydrated core) and diffusion of the drug through the hydrated matrix (**Figure 2**).

Figure 1. Carbopol® Polymers Hydration Mechanism

Dry Polymer



Hydrated Polymer

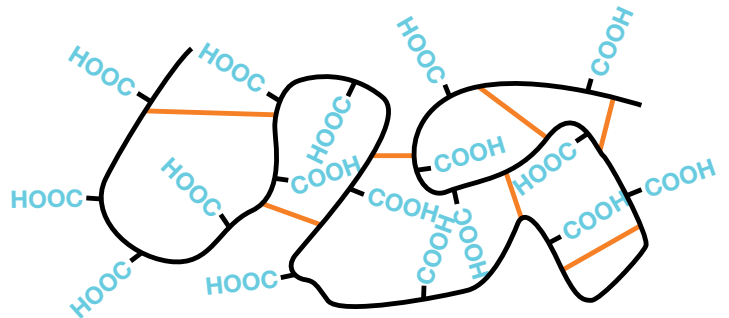
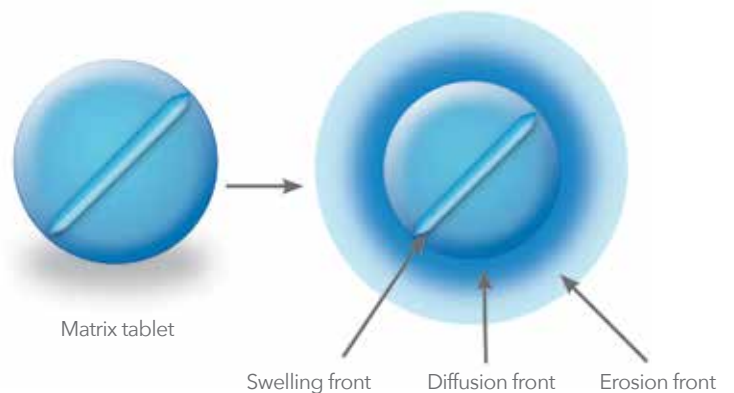


Figure 2. Drug Release Schematic





Formulation Considerations for Carbopol Polymers

There are many factors that need to be taken into consideration when formulating with Carbopol polymers, including the polymer and API highlighted below, but Lubrizol researchers support all of our partners' formulation needs through our global technical service team, which you are encouraged to contact online at any time.

Polymer Grade and Level

- Lightly crosslinked Carbopol polymers (971P NF) tend to be more efficient in controlling drug release than highly crosslinked Carbopol polymers (974P NF). Intermediate drug release can be achieved by combining Carbopol 971P NF and 974P NF polymers - **Figure 3**.
- Increasing the usage level of Carbopol tends to result in slower and more linear drug release.
- At low usage levels, due to the crosslinked nature, Carbopol polymers can be more effective than cellulose in sustaining drug release - **Figure 4**. This allows reduction in tablets size for better patient compliance.



Figure 3. Ketoprofen release in pH=6.8 phosphate buffer from tablets (200 mg) with Carbopol® polymers.

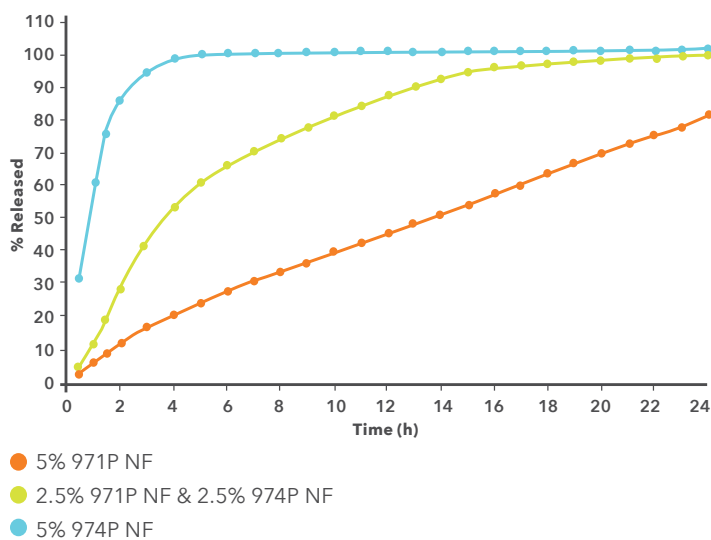
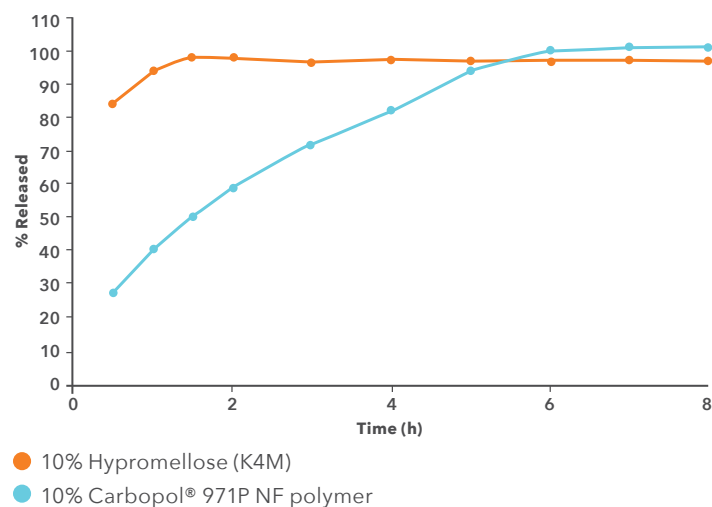


Figure 4. Guaifenesin release in 0.1 N HCl from tablets (100 mg).



API Solubility & Dose

- Higher API solubility and/or dose generally requires higher polymer levels. For water-soluble drugs, 10% powder grade polymer or 25% granular grade polymer is a good starting concentration. Lower polymer levels may be sufficient for low-solubility drugs.
- For higher-solubility/high-dose drugs, other approaches may be required in conjunction with increasing the polymer level. Examples include using a polymer combination matrix or combination of technologies (addition of the polymer intra- and extra-granularly, coating the matrix tablets, etc.).

Dissolution Medium:

- Drug release from Carbopol polymers matrices may be pH-dependent.
- At lower pH values, the polymer is not fully swollen and there are larger regions of microviscosity, resulting in faster drug release. As the pH increases, the ionization of the carboxylic acid groups causes maximum swelling, resulting in fewer and smaller regions of microviscosity and slower drug release.
- However, it is important to note that the pH effect on the polymer does not significantly impact drug release in various media. The most significant factor impacting drug release is API solubility and how it is affected by pH. Lubrizol has demonstrated that Carbopol polymers have the ability to form robust tablets which can extend drug release in both acid and buffer media. No significant difference has been observed in the release profiles due to dissolution medium in the case of drugs with pH-independent solubility.

Bioadhesion / Mucoadhesion Properties

- Carbopol polymers and Noveon polycarbophil can provide bioadhesive properties. Extensive published data and examples of commercial products are available to support this application.

Taste Masking Properties

- Carbopol polymers can mask the taste of some APIs (mostly cationic drugs) by forming insoluble adsorbates through weak ionic bonding. These adsorbates dissolve rapidly after ingestion (the endogenous cations displace the drug from the polymer). Literature references highlighting this property encompass APIs such as macrolide antibiotics, enrofloxacin, and dextromethorphan.
- Carbopol polymers have been used in combination with film-forming materials for taste-masking coating compositions. Additionally, Carbopol polymers have been reported to ameliorate the throat catch (unpleasant taste and sensation in the throat) caused by drugs such as ibuprofen. Possible mechanisms involve binding to specific sites in the throat or coating the mucosa to prevent contact of the bitter and/or throat catch producing agent with the mouth and throat mucosa.

Floating Tablets Application Properties

- Carbomers do not dissolve and are not metabolized in the gastrointestinal tract. In gastric medium, the polymers hydrate and swell, enabling floating. Carbomers can be used alone or in combinations with other polymers or effervescent systems to formulate gastric floating dosage forms.





API Assay

In order to ensure total recovery of the API from the Carbopol polymer tablets, it is recommended to run analysis after grinding the tablets. Key considerations are as follows:

- API extraction - API is extracted from the crushed tablets by sonication or other mixing techniques.
- Solvent selection - API solubility and reduced polymer swelling are criteria when selecting a solvent. Examples of solvents in which the polymer does not swell extensively are anhydrous ethanol or an acidic aqueous solution at pH ~1.2.
- Optimizing the extraction method - generally larger solvent volume and longer sonication time improves API recovery, but these have to be tested to determine if they affect API stability.
- Addition of an electrolyte - the addition of an electrolyte (sodium chloride) to the extraction solvent may improve the recovery (ion effect on the polymer).

Stability and Packaging Considerations Carbopol Polymer Matrix Tablets

- Carbopol polymers are hygroscopic materials, and packaging of tablets containing the polymers should provide moisture protection. It is recommended that the stability of the final product should be evaluated as part of the formulation development activities.

Processing Considerations

Table 2			
Method of Tablet Manufacture	Recommended Grade	Typical Polymer Levels	Formulation/Processing Considerations
Direct Compression	Carbopol® 71G NF	10-30%	<ul style="list-style-type: none"> • Carbopol has excellent binding properties (compressibility). Powder grades have very fine particle size and static charge (thus not free-flowing). • Carbopol 71G NF is in granular form and has good flowability. Therefore, it can be processed easier than the powder form of Carbopol. • Powder grades of Carbopol are more efficient in extending drug release than the granular grade due to the larger surface area, thus lower levels of polymer are generally needed. • Varying the compression forces to achieve acceptable hardness generally does not significantly affect the drug-release characteristics. • Segregation may occur in the powder blend. Separation might be prevented by preblending the API and polymers using ingredients with similar particle size distribution and density or by achieving ordered mixing. • APIs with poor flowability or compressibility can be granulated and the granules blended with Carbopol.
	Carbopol® 974P NF	3-5%	
	Carbopol® 971P NF	3-5%	
	Noveon® AA-1 Polycarbophil	3-5%	
Nonaqueous Granulation	Carbopol® 974P NF	5-25%	<ul style="list-style-type: none"> • The advantage of using Carbopol in nonaqueous solvents is to avoid rapid swelling of the polymer, which facilitates processing. • Nonaqueous granulation is possible at Carbopol levels greater than 10% of the blend, when aqueous granulation may be more challenging. • Ethanol and isopropyl alcohol can be used as granulating solvents. The swelling of Carbopol polymer is faster in ethanol than in isopropyl alcohol. • Avoid contact with water and moisture (control relative humidity, use dry equipment).
	Carbopol® 971P NF	5-25%	
	Noveon® AA-1 Polycarbophil	5-25%	
Aqueous Granulation (High/Low Shear)	Carbopol® 974P NF	5-10%	<ul style="list-style-type: none"> • Controlled release can be efficiently achieved at low levels (5%-10%) due to the large surface area of the powder-grade polymer. Higher levels (up to 20%) may be processed, if needed. • Generally, it is recommended to incorporate the polymer in the powder blend (versus adding it as a dispersion in water) due to the high viscosity of the polymer. • Screening or combing the polymer with other ingredients is beneficial to improve dry polymer handling (compensates for static charge and fine particle size). • No additional binder is required because Carbopol polymer has good binding properties. • Incorporation of microcrystalline cellulose improves the processability of the formulation. Generally, less than 10% of microcrystalline cellulose should be used to prevent disintegration of the tablets. • In order to avoid fast and extensive swelling of the polymer, add a low amount of granulation liquid sprayed at a slow rate in fine droplets (uniform distribution of the water in the wet mass). • Granulation should be controlled in order to prevent overwetting (sticky, rubbery mass). • The amount of granulation liquid used is typically lower than that expected for cellulosic polymers. • It is very important to control the drying process and residual moisture in the granules (typical values 1%-3%); however, these parameters are formulation-specific. If overdried, Carbopol polymer forms hard granules. High residual moisture might lead to tablets sticking to the punches and stability problems. • Varying the compression forces to achieve acceptable hardness generally does not significantly affect the drug-release characteristics.
	Carbopol® 971P NF	5-10%	
	Noveon® AA-1 Polycarbophil	5-10%	

Processing Considerations

Table 2 (Continued)			
Method of Tablet Manufacture	Recommended Grade	Typical Polymer Levels	Formulation/Processing Considerations
Fluid Bed Granulation	Carbopol® 974P NF	5-10%	<ul style="list-style-type: none"> Carbopol polymer has small particle size, static charge and low density, therefore precautions need to be taken during granulation. The fluidization should be kept low at the beginning of the process to prevent adherence of Carbopol polymer to the filter bag. The spray rate should be controlled to prevent formation of large, overwet agglomerates.
	Carbopol® 971P NF	5-10%	
	Noveon® AA-1 Polcarbophil	5-10%	
Dry Granulation (Roller Compaction)	Carbopol® 974P NF	3-20%	<ul style="list-style-type: none"> Roller compaction avoids rapid polymer swelling in water. It is recommended to blend all of the ingredients except the lubricant prior to compaction to achieve slower release rates. The formulation does not need an additional binder when Carbopol polymer is included. For example, Carbopol 71G NF polymer is currently manufactured by roller compaction of Carbopol 971P NF polymer with no additives. The polymer properties are not affected by multiple compaction steps.
	Carbopol® 971P NF	3-20%	
	Noveon® AA-1 Polcarbophil	3-20%	
Extrusion Spheronization	Carbopol® 974P NF	5-20%	<ul style="list-style-type: none"> Carbopol polymer must be used with microcrystalline cellulose in order to reduce the tackiness of the wet mass and facilitate processing. Extrusion spheronization using water is possible and recommended versus a solution of electrolytes. The amount of water, extrusion speed, spheronization speed, and time need to be optimized in order to obtain the highest yields and sphericities. In the presence of electrolytes (e.g., calcium chloride), the processing is easier, but the electrolyte has a negative consequence on the bioadhesion and drug release.
	Carbopol® 971P NF	5-20%	
	Noveon® AA-1 Polcarbophil	5-20%	
Hot Melt Extrusion	Carbopol® 974P NF	5-20%	<ul style="list-style-type: none"> Carbopol polymer can be used in combination with thermoplastic materials. The method is also suitable to obtain solid dispersion of low-solubility APIs.
	Carbopol® 971P NF	5-20%	
	Noveon® AA-1 Polcarbophil	5-20%	

Direct Compression Procedure

1.

Screening

Weigh all ingredients except the lubricant and screen them (20-45 mesh screen). Add the low-density material first and the high-density material at the end.

It is beneficial to combine materials with poor flowability, small particle size or static charge with another material in order to improve the overall handling of the powder blend. For example, it is recommended to combine powder grade Carbopol polymer with some fillers or combine an API with Carbopol 71G NF polymer.

Note: Sometimes a pre-blending step is done to facilitate screening.

2.

Mixing

Mix the powder blend to achieve content uniformity. Add the lubricant to the powder blend and mix for 2-5 minutes (avoid overmixing and overlubrication).

3.

Compression

Compress the powder blend to target weight and hardness.



Wet Granulation Procedure

- 1. Milling/Sieving**
Weigh all ingredients except the lubricant and screen/mill them (20–45 mesh). Add the low density material first and the high-density material at the end. It is beneficial to combine materials with poor flowability, small particle size or static charge with another material in order to improve the overall handling of the powder blend. For example, it is recommended to combine powder-grade Carbopol polymers with some fillers.
Note: Sometimes a pre-blending step is done to facilitate screening.
- 2. Dry Blending (low/high shear granulators)**
Mix the powder blend to achieve content uniformity.
- 3. Preparation of the Liquid Binder (agglutinant)**
This step is not generally necessary as formulation can be granulated with deionized water or solvents (no additional binder needed).
- 4. Wet Massing (low/high shear granulators)**
Granulate the powder blend with deionized water or solvents. In order to avoid fast and extensive swelling of the polymer, use a low amount of granulation liquid added at a slow rate in fine droplets (uniform distribution of the water in the wet mass). Granulation should be controlled in order to prevent overwetting (sticky, rubbery mass). Incorporation of microcrystalline cellulose improves the processability of the formulation. Generally, less than 10% of microcrystalline cellulose should be used to prevent disintegration of the tablets.
- 5. Wet Screening**
Pass the wet mass through a screen (6-12 mesh).
- 6. Drying of the Granules**
Dry the granules in an oven or in a fluid bed dryer until residual moisture is approximately 1.5%. If overdried, Carbopol polymers forms hard granules. High residual moisture might lead to tablets sticking to the punches and stability problems.
- 7. Screening of the Granules**
Pass the granules through a screen (16–20 mesh) to break down any agglomerates formed during drying.
- 8. Mixing of the Granules with Extragranular Components**
Add the lubricant to the granules and mix for 2–5 minutes (avoid overmixing and overlubrication).
- 9. Compression**
Compress the granules to the target weight and hardness.

Dry Granulation Procedure (Roller Compaction)

- 1. Milling/Sieving**
Weigh all ingredients except the lubricant and screen/mill them (20–45 mesh). Add the low-density material first and the high-density material at the end.
- 2. Mixing**
Mix the powder blend to achieve content uniformity.
- 3. Compaction**
Compact the powder blends and control the process parameters (feed rate, compaction pressure, roll speed, roll gap).
- 4. Sizing**
Size the ribbon to the target particle size. If necessary, recycle the over- and under-sized-material.
- 5. Mixing With Extragranular Components**
Add the lubricant to the granules and mix for 2–5 minutes (avoid overmixing and overlubrication).
- 6. Compression**
Compress the granules to the target weight and hardness.





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About Lubrizol Life Science Health

The Health business team partners with customers to speed their innovative medical devices and differentiated pharmaceutical products to market. Our dedicated team provides best-in-class polymers and excipients, along with state-of-the-art product design, development, and manufacturing services, with the ultimate goal of creating solutions that improve patient outcomes.

For more information, visit lubrizol.com/Health



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