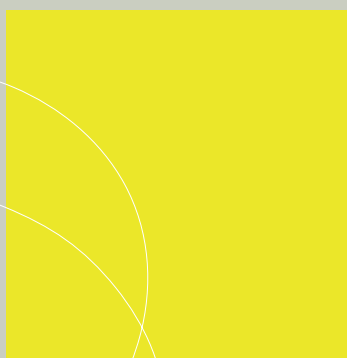


MEETING YOUR CHALLENGES
TODAY AND TOMORROW



Avicel PH

BINDERS

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AVICEL PH

Solving problems begins with understanding their origin

FMC BioPolymer understands the dynamics of the pharmaceutical industry.

We recognize the challenges you face in product development and patent strategy.

We are fully aware how important speed to market has become and how challenging factors like market fragmentation can be.

We accept these challenges as our own and are committed to helping our customers overcome them.

We are passionate about enhancing your responsiveness to changes in the market.

And we are continually looking for new ways to help you operate more efficiently and more profitably.

We are FMC BioPolymer.

We formulate solutions.



FUNCTIONALITY AND CONSISTENCY

No excipient has a greater influence on tableting success than the choice of tablet binder. Which is why Avicel PH has been the binder of choice for pharmaceutical tablets for over 40 years.

Avicel PH is a purified, partially depolymerized cellulose made by acid hydrolysis of specialty wood pulp controlled to an even more stringent degree of polymerization (DP) than required by global pharmacopoeiae. Avicel microcrystalline cellulose is made exclusively from premium select, high-purity alpha-cellulose wood pulps, with a stable supply guaranteed by long-term contracts. And it is backed by an extensive network of technical support, including FMC's compaction simulator research group.

The result is a highly functional, reliable, flexible, and free-flowing binder offering outstanding compression, binding, and disintegration properties.

Avicel PH Characteristics	Benefits
<ul style="list-style-type: none"> • Top-quality raw materials • Long-term supplier contracts • Non-genetically modified 	<ul style="list-style-type: none"> • Secure supply, superior functionality, purity, and consistency • Regulatory consumer acceptability
<ul style="list-style-type: none"> • FMC spray-drying expertise 	<ul style="list-style-type: none"> • More homogenous particles with a rounder, more porous morphology • Superior compaction, flow, and anti-segregation properties • High specific surface area adds to overall functionality
<ul style="list-style-type: none"> • Pharmaceutical grade • Stringent manufacturing standards 	<ul style="list-style-type: none"> • Tighter specifications than monographs governing NF, Ph.EUR, and JP • Unrivaled consistency and validated processes allow for reduced sampling and testing
<ul style="list-style-type: none"> • Versatile • Performs consistently • Enables robust formulations 	<ul style="list-style-type: none"> • Time and cost savings • Facilitates efficient formulation development and production • Speeds scale-up and product launch
<ul style="list-style-type: none"> • Dual-sourcing from U.S./Europe • Dedicated GMP facilities 	<ul style="list-style-type: none"> • Ensures secure and reliable global supply • Eliminates cost of approving second supply source
<ul style="list-style-type: none"> • FMC technical support 	<ul style="list-style-type: none"> • Shorter product development cycle • Optimized product formulation • Increased productivity gains



APPLICATIONS

Optimizing performance

Direct compression

Avicel PH offers a wide range of versatile grades, giving you the flexibility to meet every formulation challenge — from R&D through production. Although several different Avicel PH grades may be successfully utilized in each of the following applications, here are our recommendations for optimal performance.

Due to their porous morphology allowing ordered mixing with micronized drug, high-flow Avicel PH-200 and Avicel PH-302 are ideal for direct compression.

- Unparalleled bonding and carrying capacity
- High dilution potential (higher drug levels)
- Water-wicking, rapidly disintegrating tablets, ideal for immediate release
- High tablet hardness at low compaction pressures
- Low tablet friability
- Low lubrication requirements
- Anti-adherent

For in-depth technical information on solid dosage form manufacturing, request a copy of our "Problem Solver and Reference Manual" by emailing us at pharm_info@fmc.com



Wet granulation

Avicel PH-101 and PH-301 enhance all aspects of the granulation process.

- Quick, even wetting and wicking
- Improves wet mass consistency, reducing the risk of over-wetting
- Reduces energy and granulation fluid inputs
- Reduced process sensitivity
- Easier screening and drying
- Reduced migration of solubles
- Reduced risk of drug-release problems due to over-granulation

To further boost the compactability of the compression mix, add extra-granular Avicel PH-200 or Avicel PH-102 SCG.

Dry granulation

For roller compaction applications, we recommend the use of Avicel PH-105.

- Strong, dry binder
- Good ribbon former
- Less fines on milling
- Effective API carrier
- Water-wicking, disintegration properties

To further boost compression mix compactibility, add extra-granular Avicel PH-200, Avicel PH-102 SCG, or Avicel PH-302.



Hard capsules

Use Avicel PH-200 or Avicel PH-302 to maximize flow for powder fill.

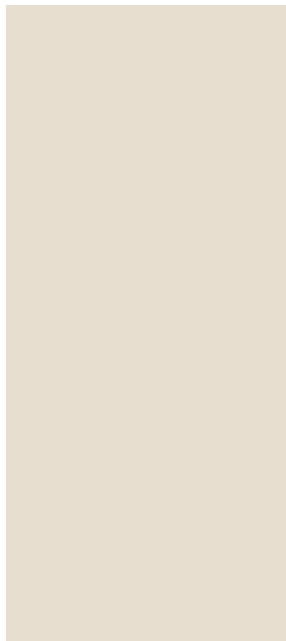
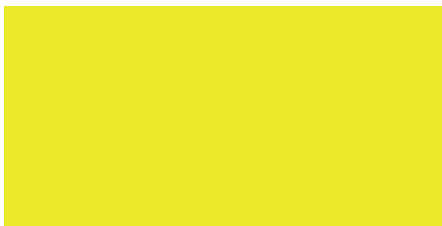
- Flow aid
- Effective API carrier
- Ideal morphology for ordered mixing with micronized drug
- Filler
- Low lubrication requirements

Extrusion/ spheronization

Avicel PH is the ideal spheronization binder and can be employed in a simple binary mixture with a drug at levels from 20% to 80%. We recommend Avicel PH-101 or PH-102 as a starting point for this application.

- Outstanding binder
- Not sticky
- Strong hydrogen bonding properties
- High carrying capacity
- Physically stable, non-disintegrating spheroids, ideal for precision coating

Customer Quote: "Using Avicel gives my formulation more robustness. I know I'm on safe ground."





Product grades

Every Avicel PH grade comes with the same high quality, the same batch-to-batch consistency, the same problem-free performance, and the same global service network.

Working together, we can help you choose the Avicel PH grade that will create cost and production efficiencies during all phases of product development and manufacturing.

	Product Grades	Nominal Particle Size, μm	Moisture, %	Loose Bulk Density, g/cc
Wet Granulation	Avicel PH-101	50	3.0 to 5.0	0.26 - 0.31
Direct Compression	Avicel PH-102	100	3.0 to 5.0	0.28 - 0.33
Superior Compactibility	Avicel PH-105	20	NMT* 5.0	0.20 - 0.30
Superior Flow	Avicel PH-102 SCG*	150	3.0 to 5.0	0.28 - 0.34
	Avicel PH-200	180	2.0 to 5.0	0.29 - 0.36
High Density	Avicel PH-301	50	3.0 to 5.0	0.34 - 0.45
	Avicel PH-302	100	3.0 to 5.0	0.35 - 0.46
Low Moisture	Avicel PH-103	50	NMT 3	0.26 - 0.31
	Avicel PH-113	50	NMT 2	0.27 - 0.34
	Avicel PH-112	100	NMT 1.5	0.28 - 0.34

*Special Coarse Grade

*Not More Than

CHALLENGES/ SOLUTIONS

The answer to your
unique challenges

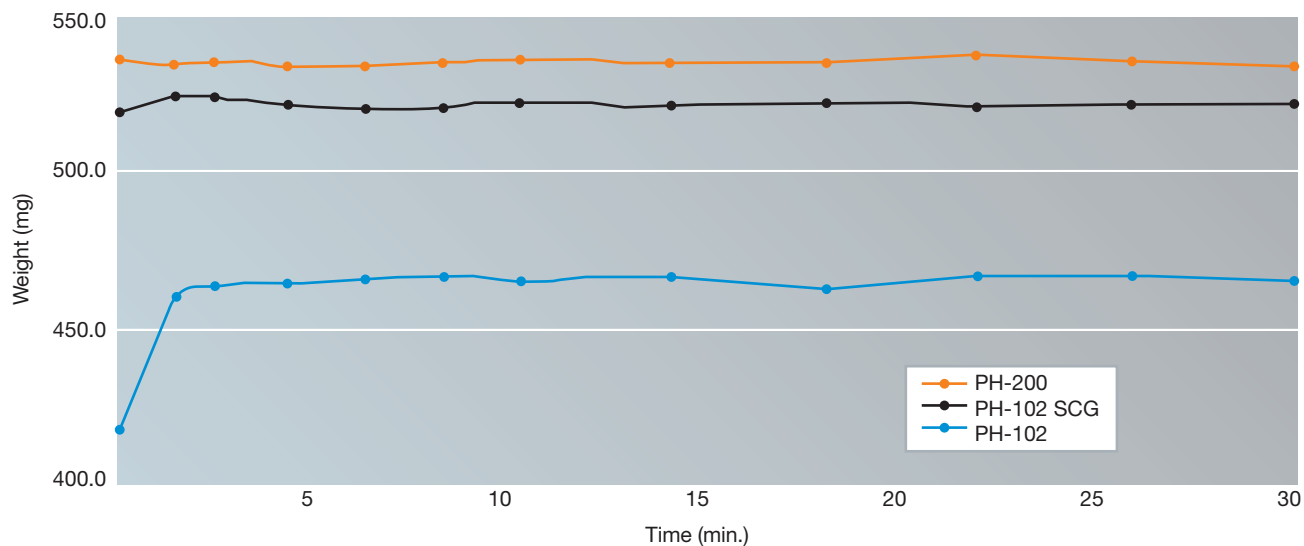
Improving flow

Avicel PH-200, Avicel PH-102 SCG, Avicel PH-302

Particle size is a key factor in determining dissolution rate, bio-availability, content uniformity, and flow. Large-particle Avicel PH-200 or PH-102 SCG can be used to improve flow and reduce tablet weight variation. Content uniformity is maintained because the porous morphology allows for ordered mixing. By improving flow, Avicel PH-200 speeds production and increases efficiency, thereby reducing production costs. Use Avicel PH-302 to boost mass flow where a smaller particle size is required.

In a test designed to measure the relative flow properties of Avicel PH-200, Avicel PH-102 SCG, and Avicel PH-102, a rotary tablet press was employed using constant die volume. As figure 1 shows, tablet weight was higher with Avicel PH-200, reflecting the increased die fill efficiency (**figure 1**).

Figure 1. Increased die fill with higher-flow Avicel PH



The die volume remained constant for each trial.



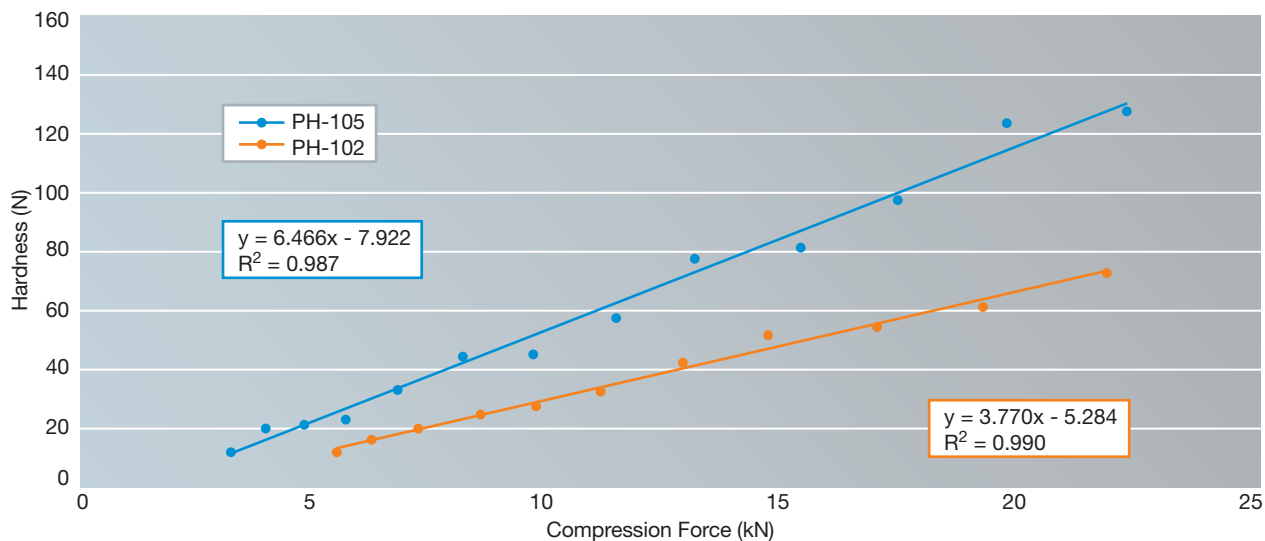
Maximize tablet strength at low binder levels

Avicel PH-105

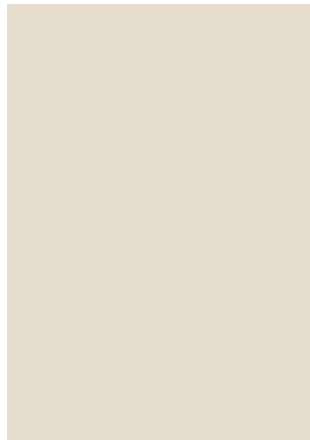
At high drug loadings, Avicel PH-105 is the low-level, high-efficiency direct compression binder of choice. It has the highest compactibility of any Avicel PH grade due to its smaller particle size, which increases bonding surface area. This allows formulators to increase

tablet strength without resorting to higher compression forces — an advantage when working with temperature- and pressure-sensitive actives. Figure 2 demonstrates how, using poorly compressible ascorbic acid, Avicel PH-105's superior compactibility enabled formulators to create tablets of greater hardness with reduced compression forces (**figure 2**).

Figure 2. Compactibility of Avicel PH-105 vs. PH-102 (39.5% Avicel, 60.0% vitamin C, 0.5% magnesium stearate)



Data generated by ESH compaction simulator.



NATURE
WORKS
SCIENCE



Moisture-sensitive actives

Avicel PH-112, Avicel PH-113, Avicel PH-103

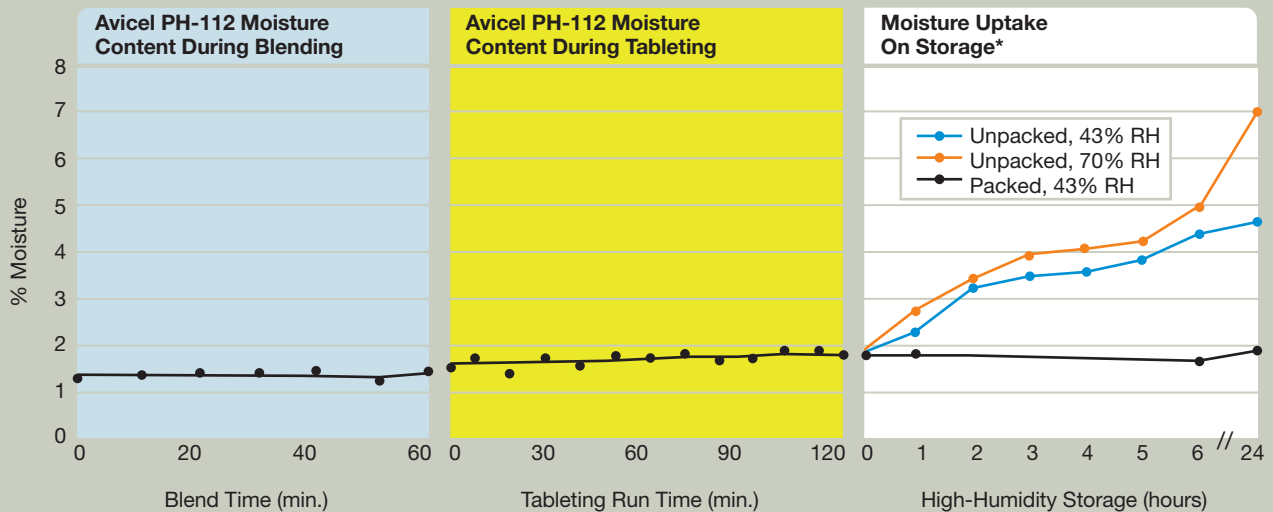
If the moisture content of Avicel PH-101 or 102 (3-5%) exceeds what is tolerable for your moisture-sensitive active, FMC offers a range of low-moisture Avicel PH grades. With proper attention to the kinetics of moisture re-equilibration, you can enjoy the benefits of low-moisture processing without the capital investment of a low-humidity facility (**figure 3, below**).

Boost production efficiency by maximizing output

Avicel PH-302, Avicel PH-301

Replacing Avicel PH-101 or 102 with Avicel PH-301 or 302, respectively, will increase the blender fill weight and boost batch tablet yield by up to 30%. In addition, these grades increase tablet weight uniformity, even at high tablet speeds (**figure 4, opposite**).

Figure 3. Moisture content during a typical tableting process for Avicel PH-112



*No significant moisture uptake was observed during blending or tableting under ambient conditions. Package immediately with an adequate moisture barrier to lock in the low-moisture benefit.

Figure 4. Tablet weight variation
(% coefficient of variation, unlubricated)

	Avicel PH-101	Avicel PH-301	Avicel PH-102	Avicel PH-302
Stokes™ B-2 Compressing Machine at 42 rpm	4.9	1.3	3.4	1.5
Manesty® Express Compressing Machine at 60 rpm	19.1	5.3	7.2	2.9



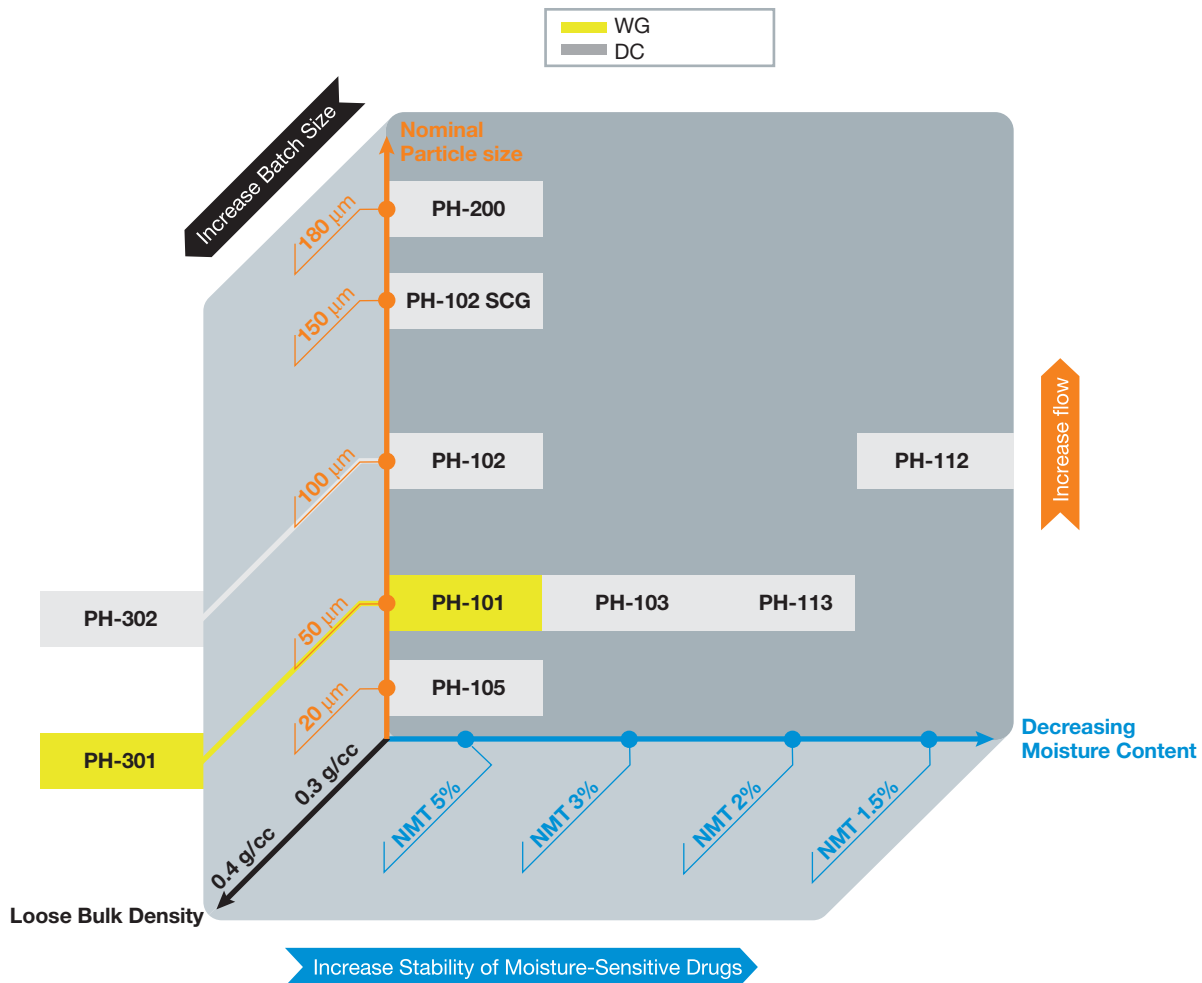
SELECTING GRADES

Choosing the Avicel PH grade that's right for your unique formulation

Avicel PH grades selection grid

There are many parameters that need to be taken into consideration when formulating a new tablet or capsule product. Figure 5, below, will help you select the appropriate Avicel PH grade to meet and overcome the challenges that are unique to your formulation. (figure 5).

Figure 5. Avicel PH selection grid



NMT= Not More Than



The right time to discover the possibilities

Backed by FMC's global service and support network, we stand ready to support the endeavors of our customers in any way possible.

Working together, we can tap the full potential of Avicel's many specialty grades. Working together, there's almost no limit to what we can achieve.

Talk to us and discover what's possible.

Regulatory

Avicel microcrystalline cellulose meets the standards set forth in the United States Pharmacopoeia/National Formulary, the European Pharmacopoeia, the Japanese Pharmacopoeia, and the British Pharmacopoeia.

Microcrystalline cellulose is generally recognized as safe (GRAS) by qualified experts. FMC maintains a Type IV Drug Master File at the U.S. Food and Drug Administration.

Nature, Humans, Science photography shot on location by: Jake Chessum. Alex Williams/JDK Photo Studio.



INNOVATION
DELIVERS
RESULTS



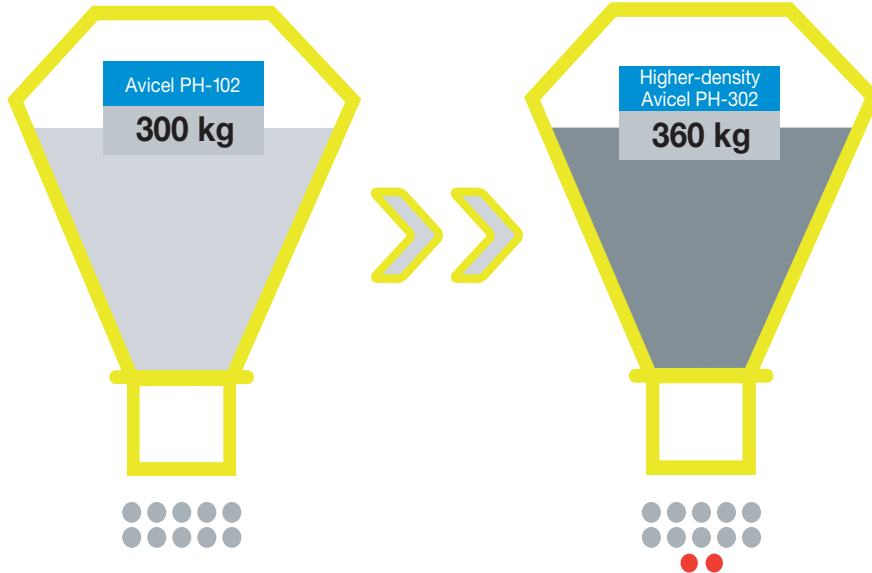
Avicel PH
Customer Case Studies

AVICEL CUSTOMER CASE #1

How Avicel PH-302 boosted production, enabling a customer to avoid a major capital investment.

A large pharmaceutical company using 60% Avicel PH-102 in direct compression was experiencing manufacturing capacity constraints due to better-than-anticipated sales of its blockbuster drug. To meet this demand, the company was contemplating significant capital investments in production capacity.

Searching for a more cost-effective alternative, the company turned to FMC. FMC suggested using higher-density Avicel PH-302 (approximately 33% denser than Avicel PH-102). The resulting 20% increase in batch weight for the same blender volume directly boosted production efficiency — without the expense of adding manufacturing capacity.



20% greater output per batch.

Results:

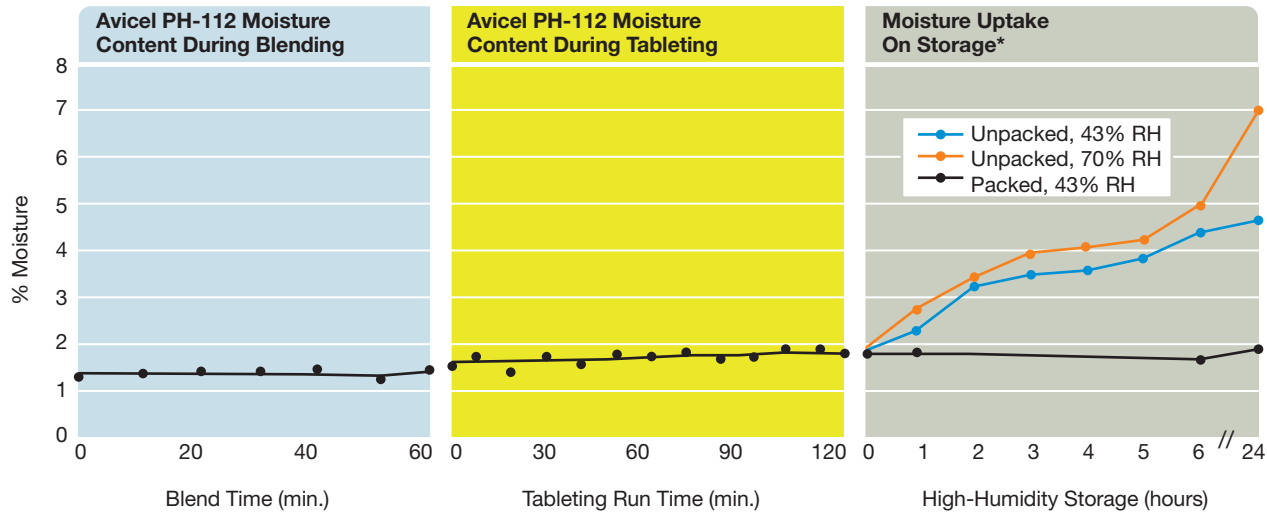
- Switching from Avicel PH-102 to higher density Avicel PH-302 enabled the manufacturer to:
- Increase output by 20%
- Save \$1M per year by improving manufacturing efficiency
- Avoid \$3-5M in capital investment

AVICEL CUSTOMER CASE #2

How Avicel PH-112 maximized drug stability for a customer.

A large pharmaceutical company approached FMC for advice on combining Avicel PH with moisture-sensitive active. First, FMC recommended a switch to the lower-moisture Avicel PH-112. FMC Technical Service then provided validation support that allowed the company to utilize Avicel PH-112 without low-humidity facilities. FMC trials confirmed that the rate of moisture uptake was not significant during normal

blending and tableting operations. To prevent moisture uptake during longer-term storage, FMC made appropriate packaging recommendations. This use of low-moisture Avicel PH-112, coupled with FMC's expertise, enabled the company to achieve stability targets without resorting to costly investments in low-humidity facilities.



*No significant moisture uptake was observed during blending or tableting under ambient conditions. Package immediately with an adequate moisture barrier to lock in the low-moisture benefit.

Results:

Using Avicel PH-112 enabled the manufacturer to:

Reach low-moisture targets

Optimize drug efficacy and stability

Avoid the costs of investing in a low-humidity facility

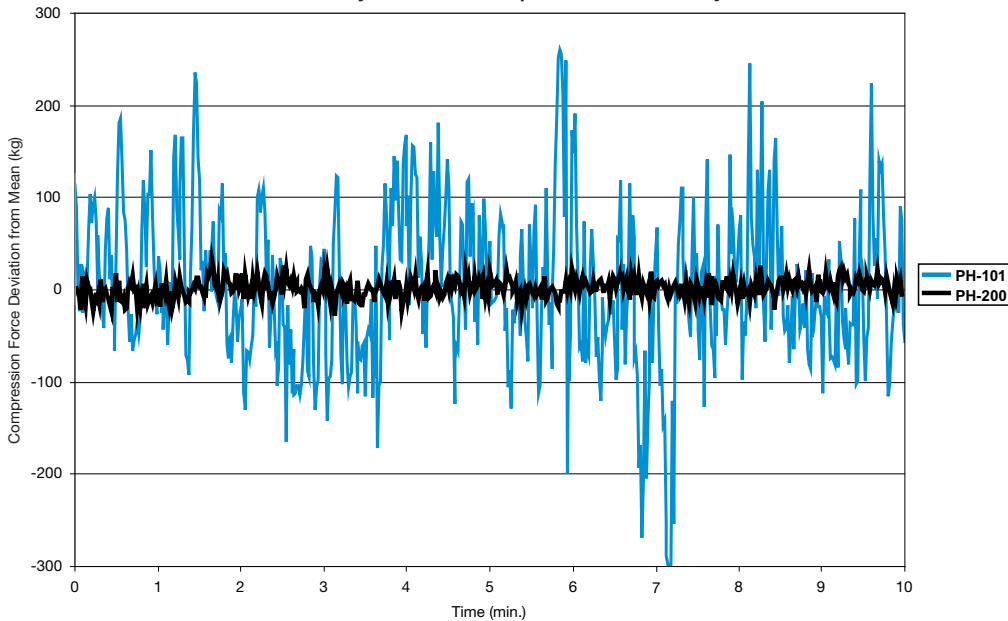
AVICEL CUSTOMER CASE #3

How Avicel PH-200 enabled a customer to improve flow and content uniformity.

A large pharmaceutical manufacturer using Avicel PH-101 was experiencing flow problems at higher production rates, resulting in variations in tablet weight. FMC Technical Service recommended replacing Avicel PH-101 with higher-flow Avicel PH-200, which eliminated the flow problems (see chart below).

As would be expected, tablet weight uniformity improved. Content uniformity also improved due to the ordered mixing between larger-particle-size Avicel PH-200 and fine active.

Avicel PH-200 vs. PH-101; Avicel PH-200 significantly improved flow as shown by the reduced compaction force variability



Results:

Switching from Avicel PH-101 to Avicel PH-200 enabled the manufacturer to:

Eliminate flow problems and increase tablet production speed

Improve weight uniformity — relative standard deviation reduced from 7% to 1.5%

Improve content uniformity — relative standard deviation reduced from 4.8% to 1.8%

Regulatory

Avicel microcrystalline cellulose meets the standards set forth in the United States Pharmacopoeia/National Formulary, the European Pharmacopoeia, the Japanese Pharmacopoeia, and the British Pharmacopoeia.

Microcrystalline cellulose is generally recognized as safe (GRAS) by qualified experts. FMC maintains a Type IV Drug Master File at the U.S. Food and Drug Administration.

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Warranty:

Because of the numerous factors affecting results, FMC BioPolymer ingredients are sold on the understanding that purchasers will make their own tests to determine suitability of these products for their particular purpose. The several uses suggested by FMC BioPolymer are presented only to assist our customers in exploring possible applications. All information and data presented are believed to be accurate and reliable, but are presented without the assumption of any liability by FMC BioPolymer.

Technical Service:

The information contained in this bulletin is intended to be general in nature. Techniques and data pertaining to specific uses for FMC BioPolymer products and new developments will be published periodically in the form of supplemental application bulletins. Our technical staff is ready to offer assistance in the use of Avicel products.

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