

**Pharma Solutions**

White Paper

# Advancing the Science of TUPs Management: Improved Process Controls, Enhanced Testing Methods and Building a Leading Brand



Off colored particles, also known as technically unavoidable particles (TUPs) or black specks, have presented challenges for pharmaceutical customers and excipient suppliers for decades. An inherent variability of standard testing and the lack of a common measurement method across the industry exacerbates this issue. Even today, the reduction of TUPs remains a common goal for customers because of the possibility of batch failures and the waste of expensive end tablet product.

DuPont has worked to tackle this challenge. An extension of its market-leading Pharma Grade Avicel® microcrystalline cellulose (MCC) excipients offers a standard lower TUPs profile. Through increased investment in advanced technologies and capabilities, we're able to measure TUPs in Avicel® MCC in a more consistent, repeatable and dependable way. This Avicel® LS line does not require re-qualification for existing Avicel® customers; it is a convenient option for customers looking to reduce TUPs visible in their products.

**Avicel® PH 101 NF LS****Avicel® PH 102 NF LS****Avicel® PH 200 NF LS****Available globally from our MCC facilities in Newark, Delaware, USA or in Cork, Ireland.**

## Solving the Specks: The Background and our Methodology

As defined by IPEC 2015 guidance, TUPs can be product and process related. Avicel® LS grade materials can demonstrate consistently lower levels of these types of TUPs:

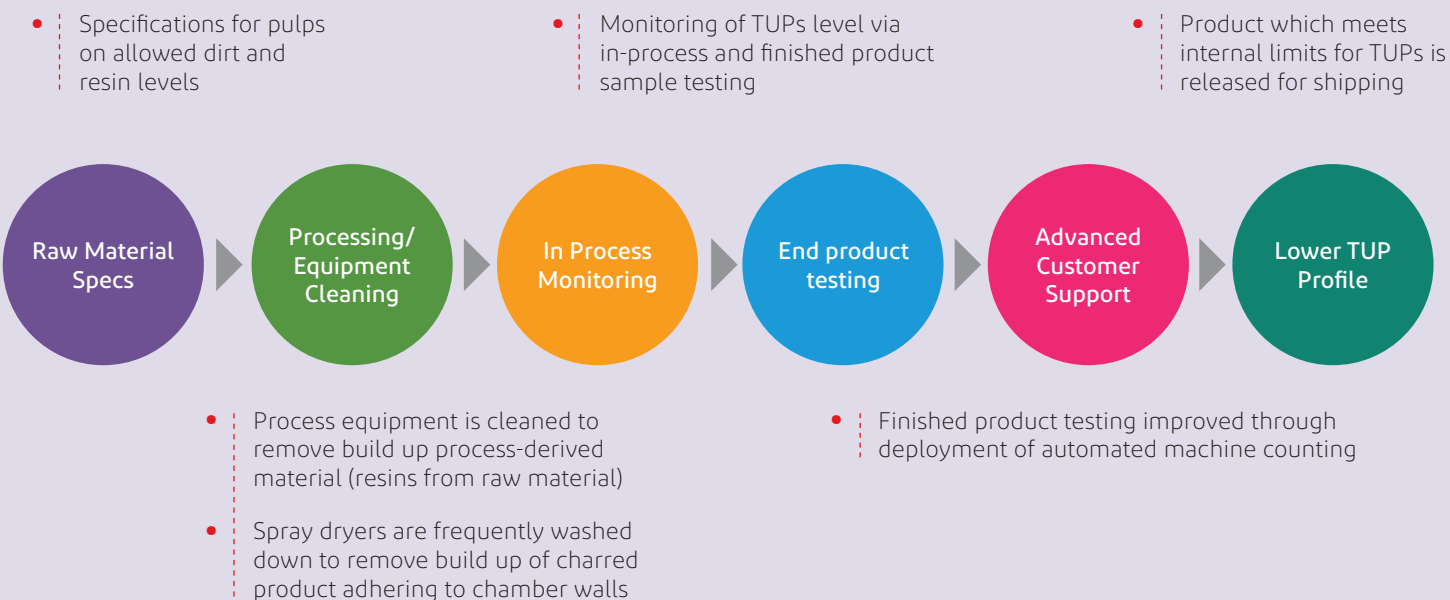
- Intrinsic components carried through from raw materials (mined materials or those sourced from natural products)
- Color variation inherent to the product
- Particles discolored due to heat (e.g. charred particles)
- Misshapen or morphologically distinct particles

## Our Approach

Pharma Solutions, a platform within DuPont Nutrition & Biosciences, uses a unique approach to reduce TUPs through integrated manufacturing, testing and support. The process starts with setting specifications for raw pulp used in Pharma Grade MCC and ends with enhanced finished product testing and customer support.

### How to minimize TUPs

World class approach to integrate product manufacturing, testing and support



## Quality and Certainty are Paramount

Using digital technology, customers can now access predictive tools to determine the probability of TUPs showing on the surface of tablet/caplet doses. The very nature of TUPs is that they're technically unavoidable, but being able to model the probability of TUPs impacting the formulation improves chances of success and reduces risk of batch loss.

Using statistics and a predictive algorithm, we've created the TUPs Calculator™, which can measure the probability of a TUPs showing up on the surface of a tablet or caplet.

Key factors modeled into the TUPs Calculator™

Specks / Gram

- Mass of Tablet
- % of MCC in Tablet
- Radius and Height of Tablet
- Radius of Specks

The TUPs calculator™ is based on the TUPs measured in a 20 Gram sample. In the case studies below, the Avicel® LS TUP Calculator measures the probability of seeing a speck on a tablet. Comparing Avicel® PH 101 NF LS to a common MCC would indicate a 73% reduction in the probability of a speck showing up on the surface of the tablet.

## Case Comparison: Common Competitive MCC vs. Avicel® LS

Tablet: 500 MG w/ 20% MCC Inclusion

### Example Competitor: Standard Grades

TUPs Calculator™

Specks/20g: 26

Mass Tablet (mg): 500

Tablet MCC (%): 20

Radius of Tablet (mm): 3

Height of Tablet (mm): 2

Radius of Specs (µm): 75



Probability of Seeing a Speck  
**2.91%**

Face Area	:	28.3mm <sup>2</sup>
Face Particles	:	1451 spheres
Side Area	:	37.7mm <sup>2</sup>
Side Particles	:	1676 spheres
Probability Spec in Pill	:	13%
Probability on Surface	:	22.36%

### Avicel® LS Grades

TUPs Calculator™

Specks/20g: 7

Mass Tablet (mg): 500

Tablet MCC (%): 20

Radius of Tablet (mm): 3

Height of Tablet (mm): 2

Radius of Specs (µm): 75



Probability of Seeing a Speck  
**0.78%**

Face Area	:	28.3mm <sup>2</sup>
Face Particles	:	1451 spheres
Side Area	:	37.7mm <sup>2</sup>
Side Particles	:	1676 spheres
Probability Spec in Pill	:	3.5%
Probability on Surface	:	22.36%

Switching to Avicel® LS would likely result in a 73% reduction in the probability of a TUP showing up on surface of tablet, generating huge savings from the reduction of failed product and batches.

Contact us today to model your formulations with the TUPs Calculator™ or to sample Avicel® LS grades.



Nutrition & Biosciences

[www.pharma.dupont.com](http://www.pharma.dupont.com)  
[www.dupontnutritionandbiosciences.com](http://www.dupontnutritionandbiosciences.com)

The information contained herein is based on data known to DuPont or its affiliates at the time of preparation of the information and believed by them to be reliable. This is business-to-business information intended for food, beverage and supplement producers, and is not intended for the final consumer of a finished food, beverage or supplement product. The information is provided "as is" and its use is at the recipient's sole discretion and risk. It is the recipient's sole responsibility to determine the suitability and legality of its proposed use of DuPont products for its specific purposes. Information and statements herein shall not be construed as licenses to practice, or recommendations to infringe, any patents or other intellectual property rights of DuPont or others.

DUPONT HEREBY EXPRESSLY DISCLAIMS (I) ANY AND ALL LIABILITY IN CONNECTION WITH SUCH INFORMATION, INCLUDING, BUT NOT LIMITED TO, ANY LIABILITY RELATING TO THE ACCURACY, COMPLETENESS, OR USEFULNESS OF SUCH INFORMATION, AND (II) ANY AND ALL REPRESENTATIONS OR WARRANTIES, EXPRESS OR IMPLIED, WITH RESPECT TO SUCH INFORMATION, OR ANY PART THEREOF, INCLUDING ALL REPRESENTATIONS AND WARRANTIES OF TITLE, NON-INFRINGEMENT OF COPYRIGHT OR PATENT RIGHTS OF OTHERS, MERCHANTABILITY, FITNESS OR SUITABILITY FOR ANY PURPOSE, AND WARRANTIES ARISING BY LAW, STATUTE, USAGE OF TRADE OR COURSE OF DEALING.

DuPont™, the DuPont Oval Logo, and all trademarks and service marks denoted with ™, SM or ® are owned by affiliates of DuPont de Nemours, Inc. unless otherwise noted. © 2020 DuPont.