PHARMA SOLID KNOWLEDGE REPORT

SYNTEGON
PROCESSING & PACKAGING

Automated Process Development (APD).

Quality by Design (QbD) was introduced by the American FDA in the ICH Q8 (R2) “as a new paradigm with significant effects on current and future trends in pharmaceutical development” (2004). QbD describes good practice for pharmaceutical product development and introduces concepts of design space and flexible regulatory aspects. It is a systematic approach to development, emphasizes product and process understanding as well as process control.

Changes in formulation and manufacturing processes during development should be looked upon as opportunities to gain additional knowledge and further possibilities for improvements (from ICH Q8 (R2)).

WHAT IS QbD?

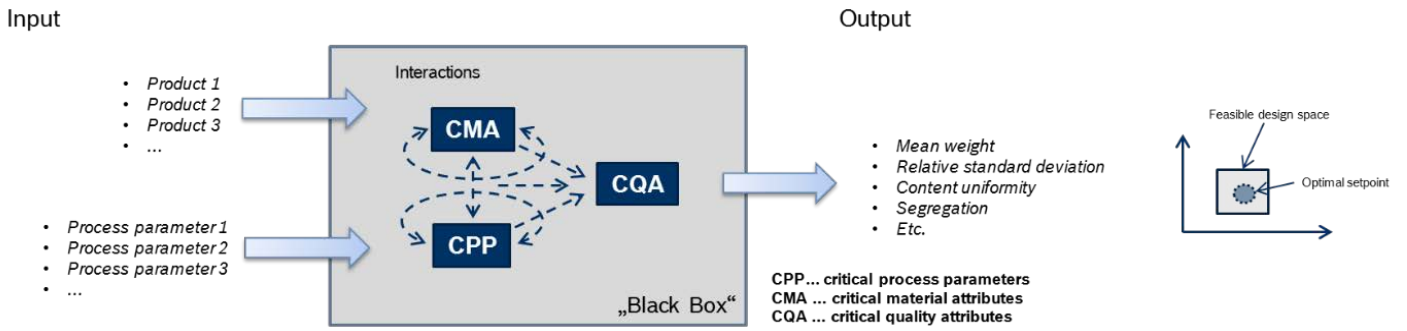
- Systematic approach to development
- Begins with predefined objectives
- Emphasizes product and process understanding and process control
- Based on sound science and quality risk management

BENEFITS OF QbD

- Enhanced process understanding
- Higher process capability
- Better product quality

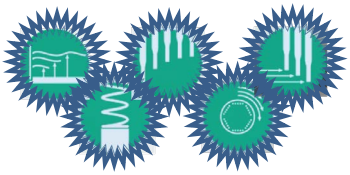
Sourcehttps://www.fda.gov/media/85369/download

CRITICAL QUALITY ATTRIBUTES AND QUALITY BY DESIGN

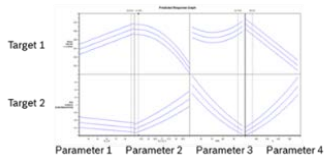


1. PLAN

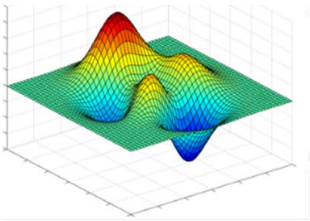
2. AUTOMATED EXECUTION



3. BUILD & ANALYZE PROCESS MODEL

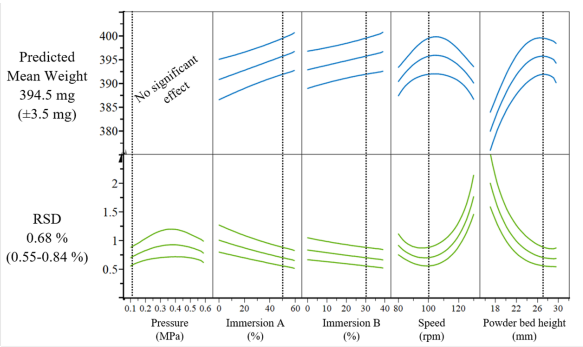


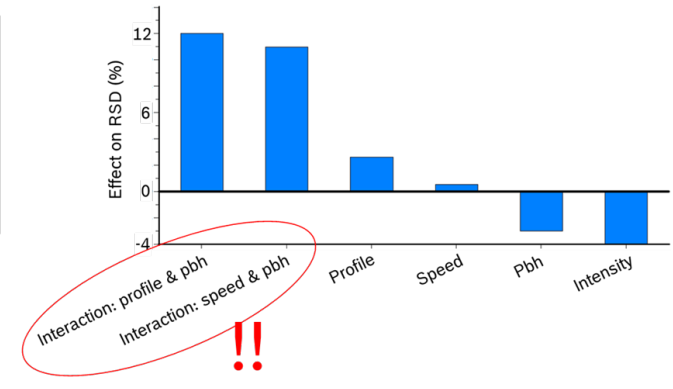
4. OPTIMIZE PROCESS & SOLVE PROBLEM



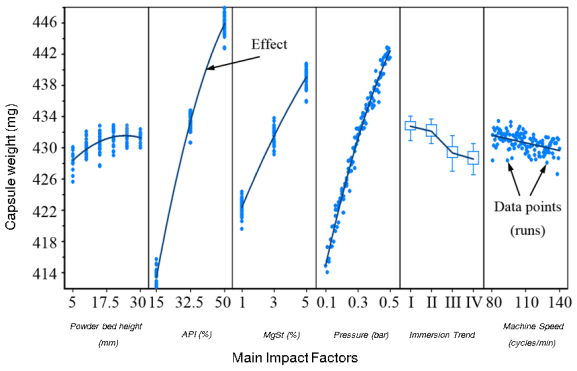
The combination of systematic planning (DoE) with automated test setup on a Syntegon GKF capsule filler is a unique and patented technology to perform many experiments in a short time. The automation allows you a broad screening to identify interactions between process parameters and to optimize yield, quality and robustness. The reproducibility of the tests and the quality of the data analysis is improved by an order of magnitude. Automation of all critical process parameters like powder bed height, pneumatic spring rate or immersion depth combined with additional PAT-sensor technology and an automation control allow a fast, efficient and powder saving execution of systematically planned experiments.

Process Optimization

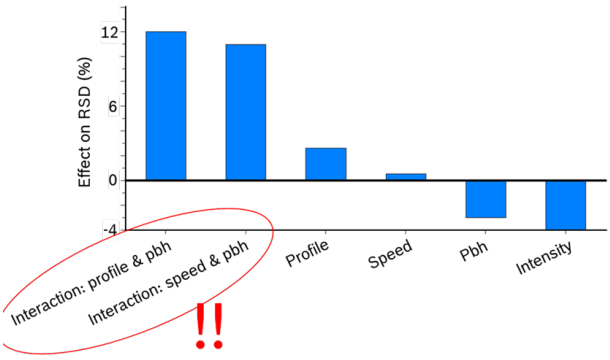


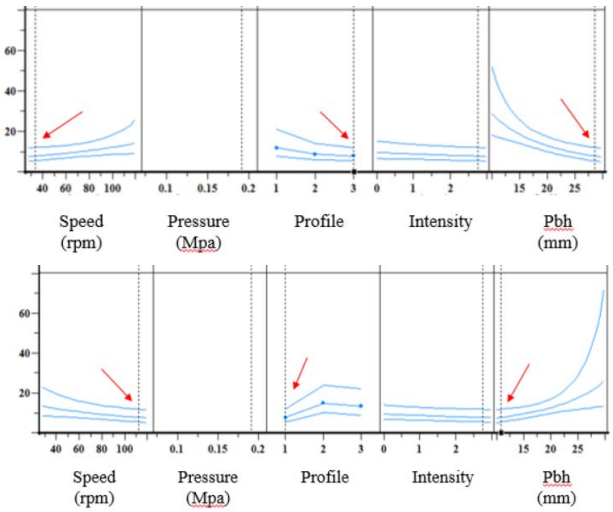


Formulation Development



Identifying Interactions and CPP



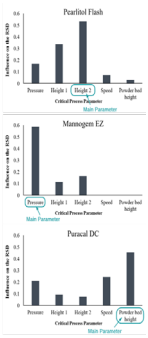


Excipient Investigation

Executed on Bosch patented GKF Setup

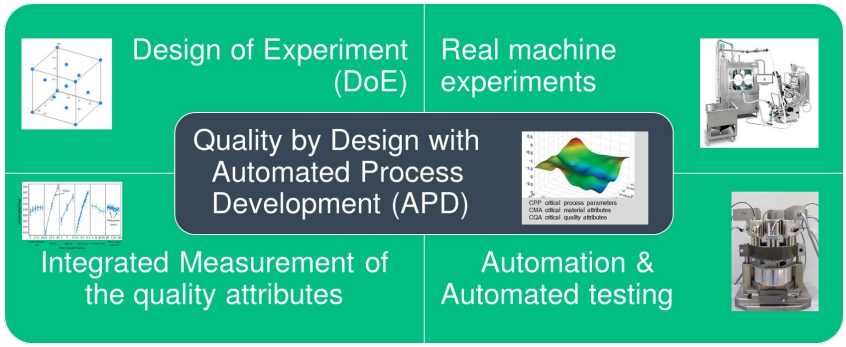
Excipient	Type	Speed (rpm)	Pressure (MPa)	Powder bed (mm)	Height 1 (mm)	Height 2 (mm)	RSD (%)
Pearlitol® Flash	Mannitol 1	120	0.08	3.1	5.0	3.1	1.1
Pearlitol® 50C	Mannitol 2	120	0.18	14.8	3.2	3.0	1.2
Pearlitol® 160C	Mannitol 3	121	0.21	15.0	3.2	5.0	1.3
Pearlitol® 200SD	Mannitol 4	96	0.08	3.0	1.0	1.8	1.3
Mannogem EZ	Mannitol 5	129	0.08	14.5	1.0	2.8	1.5
Mannogem 2080	Mannitol 6	136	0.08	3.0	1.0	3.1	1.6
Parteck M200	Mannitol 7	80	0.50	15.0	5.0	1.0	1.5
Puracal® Xpress	Calcium lactate 1	120	0.35	15.0	5.0	3.2	0.7
Puracal® DC	Calcium lactate 2	140	0.50	13.9	1.0	5.0	1.5
Puracal® PP	Calcium lactate 3	120	0.17	15.0	5.0	2.3	1.4
Calcium lactate pentahydrate	Calcium lactate 4	127	0.35	15.0	3.1	1.0	1.3
Dicalcium phosphate	Calcium phosphate 1	140	0.08	4.2	1.0	3.3	1.7

Process parameter setting: low middle high



MORE THAN 100 APD TESTS PERFORMED!

- **RSD**: RDS of difficult sticky powder with parameter interaction improved from 9% to 2%
- **Weight**: 200mg transferred from capsule size 0 to capsule size 1 by improved tamping process parameters for a fluffy product
- Increased **yield** of good capsules from 94% to 99% for difficult products
- **Tool** for targeted **scale-up-process** and ability to handle batch variability by identifying CPP's
- Coming soon: APD for micro dosing of powders
- Coming soon: APD for TPR tablet compression



Conclusion

- The Automated Process Development (APD) is a unique Syntegon approach to real Quality by Design and optimum processes
- APD allows an efficient and fast determination of Critical Material Attributes, Critical Process Parameters and Critical Quality Attributes
- Enhanced process understanding and higher product capability leads to better product quality
- Simplified and controlled scale up process

Please contact us!

Please share your difficult products and processes with us, to find optimized solutions.
Our "Engineering Pharmaceutical Service" team will be available with all our experience of over 50 years:

Dr. Thomas Brinz
Head of Department Engineering Pharmaceutical Service
Phone: +49(7151)14-2160
Thomas.Brinz@syntegon.com

Syntegon Technology GmbH
Stuttgarter Straße 130
71332 Waiblingen
Germany
Mail packaging-ph@syntegon.com
Web www.syntegon.com

facebook.com/Syntegon
twitter.com/Syntegon
youtube.com/Syntegon
linkedin.com/Syntegon

09.2020