APMF 2017

Dr.Reddy's

Modelling of Spray drying Processes using gSOLIDS – a holistic approach

- Sridevi Challa, Dr.Reddys

Acknowledgements:

Ravi Chandra Palaparthi, Dr.Reddys *Deon Pistorious, PSE*

Video courtesy: Pulse Dry Systems

OUTLINE

1

- **Introduction**
  - **Spray Drying General aspects**
  - **Typical Challenges in industry**
  - **Need for a Mechanistic model**

2

- **gSOLIDS Spray Drying Model**
  - **Overview**
  - **Workflow**

3

- **Customization done**
  - **Atomization models**
  - **Cyclone model**

4

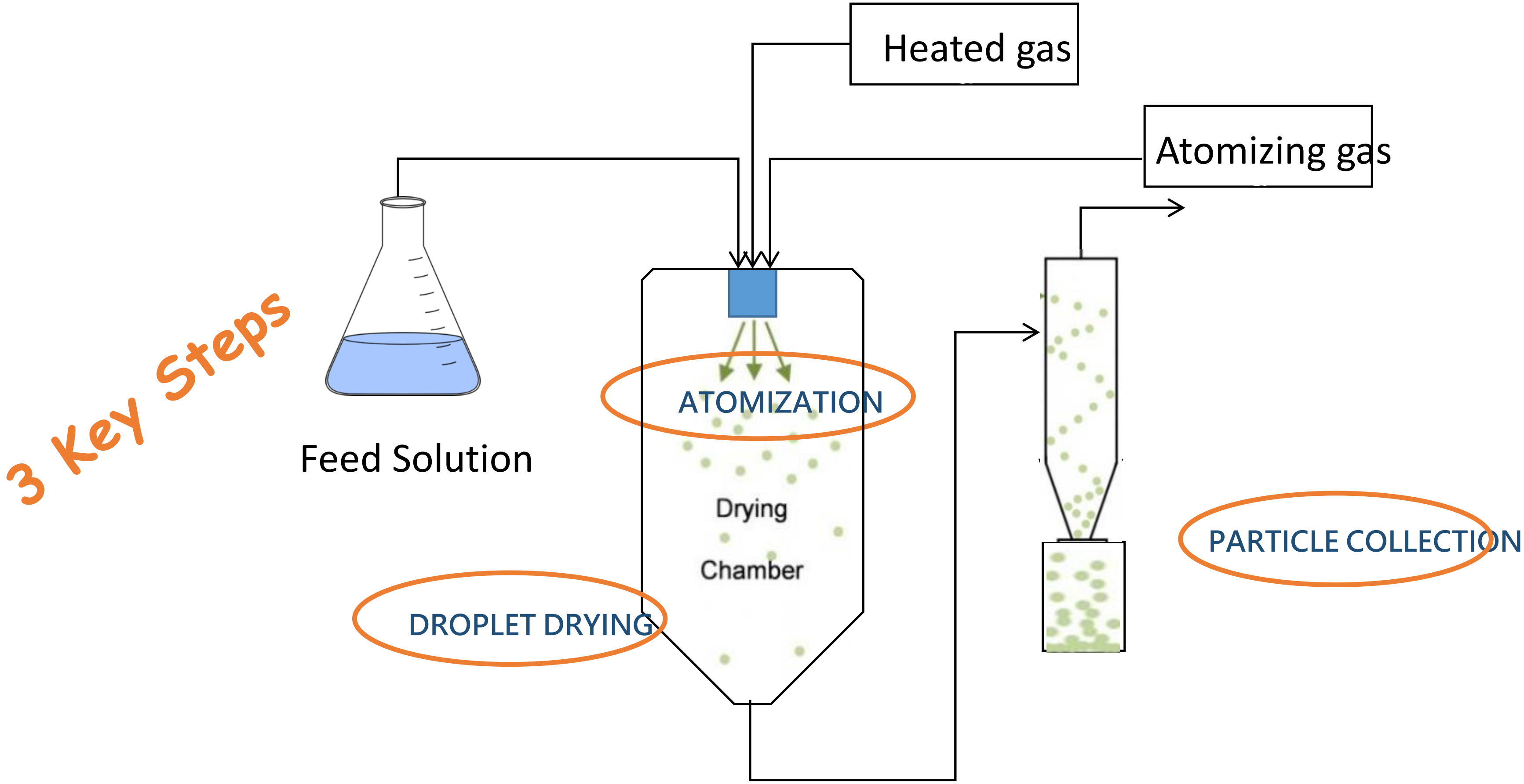
- **Case Studies**
  - **Product 1**
  - **Product 2**

5

- **Conclusion**

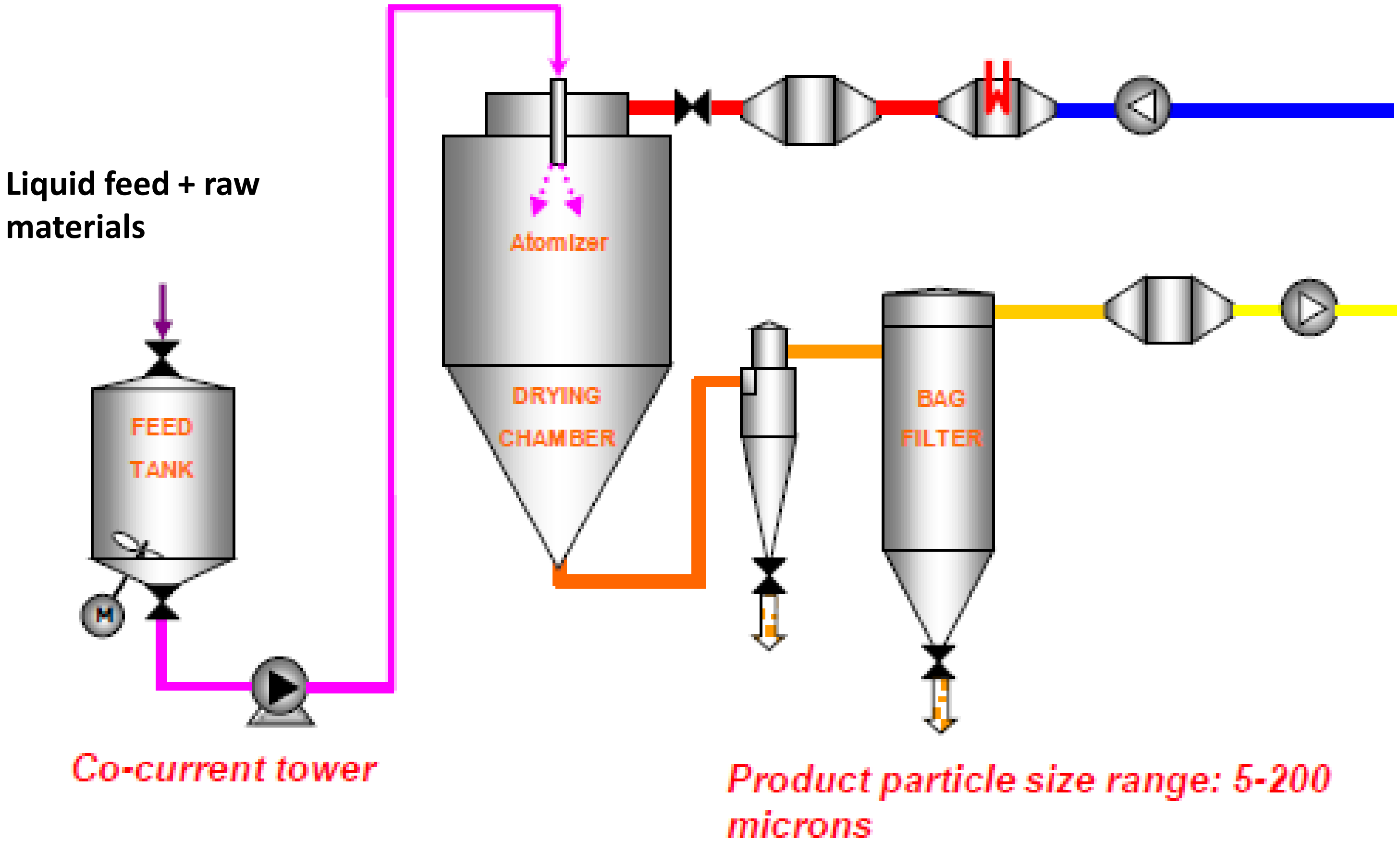
What is Spray Drying ?

Spray drying is evaporation of a liquid from a solution or suspension to give a dry powder product, by forming fine droplets and drying with hot gas



Ref: Modelling spray drying of fine particles using gSOLIDS , Thoralf Hartwig, Ian Kemp

Typical co-current spray drying process



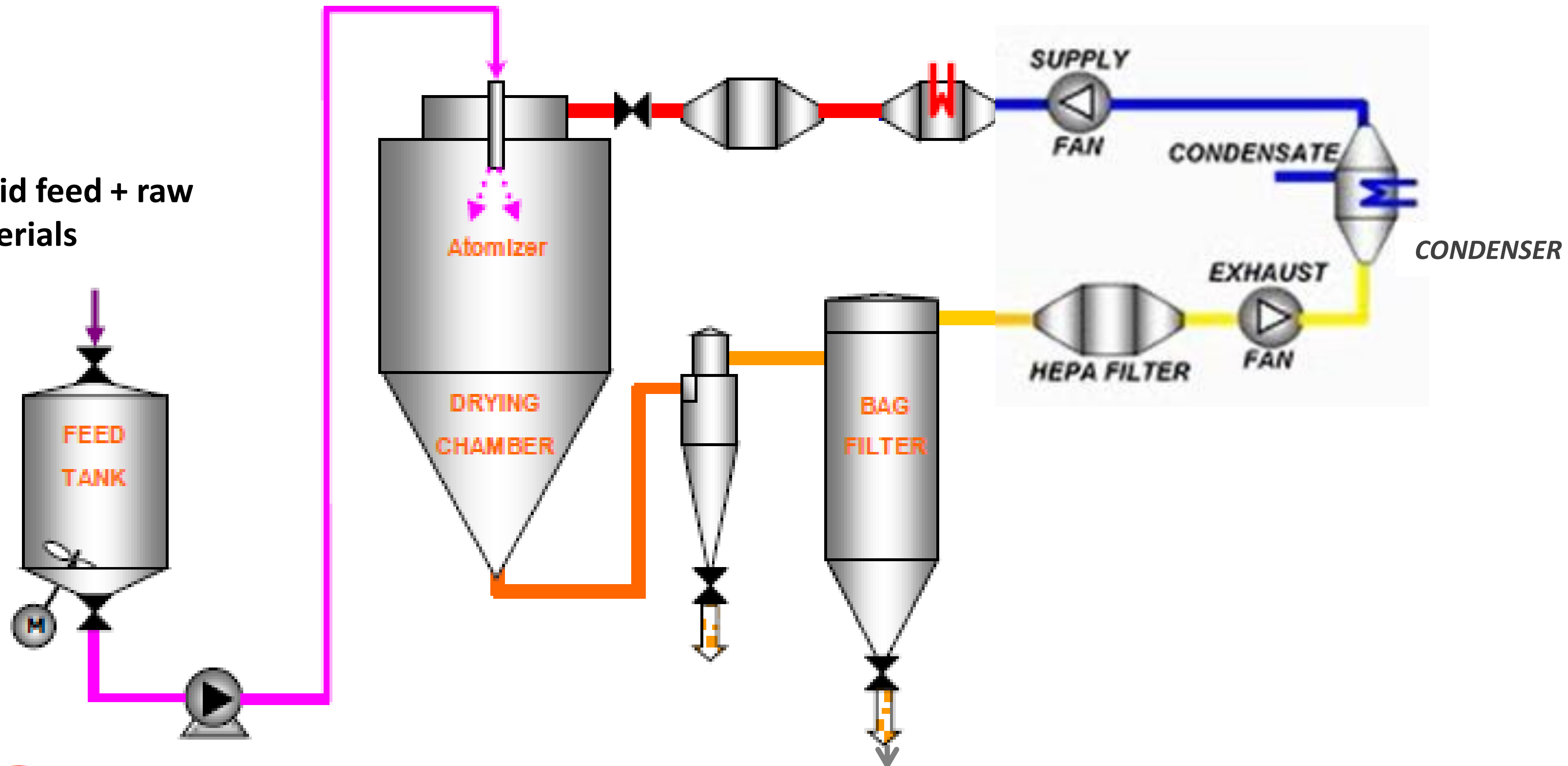
Open Loop Operation

Ref: Pinto, M.A., Bermingham, S., P. Bach, M.Nerby , 2011. Modelling of a spray drying process, AIChE Annual Meeting, Minneapolis, MN, USA.

Spray drying process with just drying gas recycle

most common type of recycle in the manufacturing of APIs….

Liquid feed + raw materials



Co-current tower

Product particle size range: 5-200 microns

Closed Loop Operation

Ref: Pinto, M.A., Bermingham, S., P. Bach, M.Nerby , 2011. Modelling of a spray drying process, AIChE Annual Meeting, Minneapolis, MN, USA.

Challenges in Spray Drying

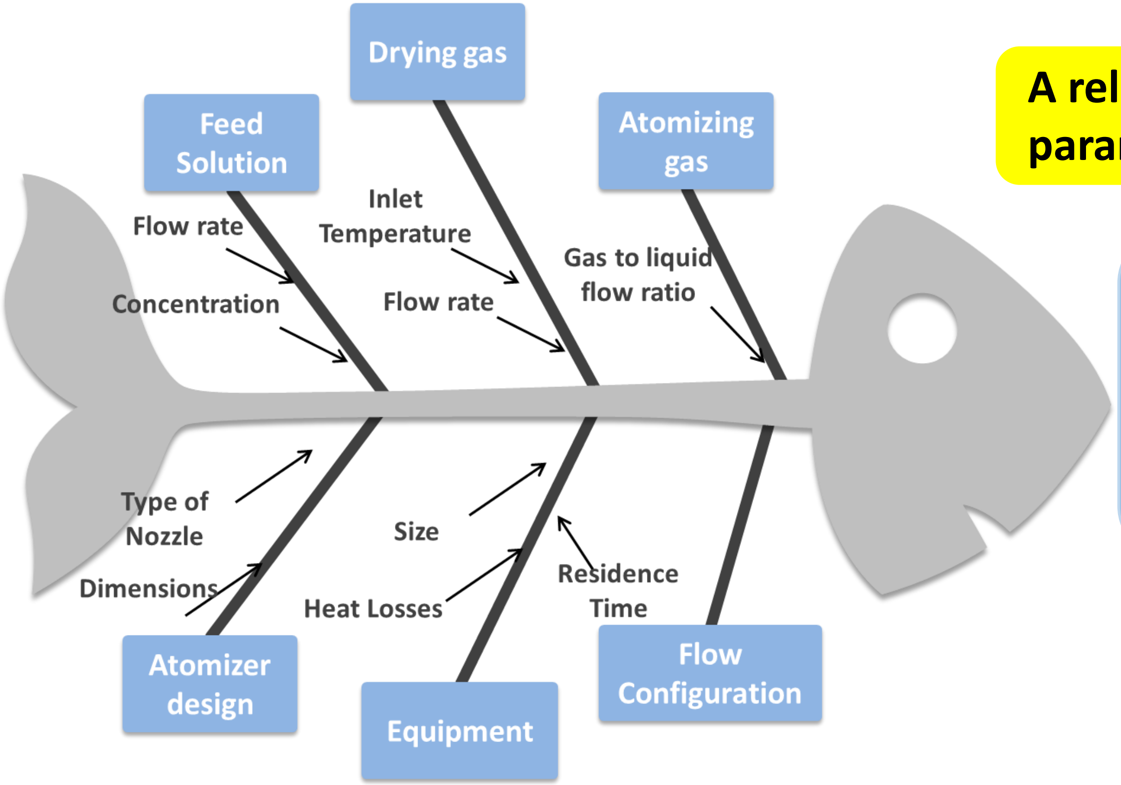
Scale Up and Process Optimization

- ❑ **Arrive at optimal spray drying conditions to achieve target particle size and residual solvent content**
- ❑ **Scale up from lab to plant scale with desired quality attributes**
- ❑ **Improve the next batch given results from previous batch**
- ❑ **Minimize equipment fouling and wall deposits to maintain yield**
- ❑ **Brand new equipment at plant scale**
- ❑ **Transfer the process across different sites.**

Image courtesy: Detroit process machinery

Ref: Pinto, M.A., Bermingham, S., P. Bach, M.Nerby , 2011. Modelling of a spray drying process, AIChE Annual Meeting, Minneapolis, MN, USA.

Why do we need a mechanistic model based approach ?



A relatively large set of process parameters that determine the CQAs

Product
- **PSD**
- **OVI**
- **Yield**

Traditional approaches use DoE to arrive at design space. DOE does not scale

Scale up based on statistical approaches is very risky.

Approaches using Mechanistic models combined with experimentation increase the confidence level during scale up !

OUTLINE

1

- **Introduction**
  - **Spray Drying General aspects**
  - **Typical Challenges in industry**
  - **Need for a Mechanistic model**

2

- **gSOLIDS Spray Drying Model**
  - **Overview**
  - **Workflow**

3

- **Customization Aspects**
  - **Atomization models**
  - **Cyclone model**

4

- **Case Studies**
  - **Product 1**
  - **Product 2**

5

- **Conclusion**

gSOLIDS Spray Drying Model - Overview

Inputs

Physical Properties of the components
- Density
- Specific heat capacity
- Thermal conductivity
- Dynamic Viscosity
- Latent heat of vaporization

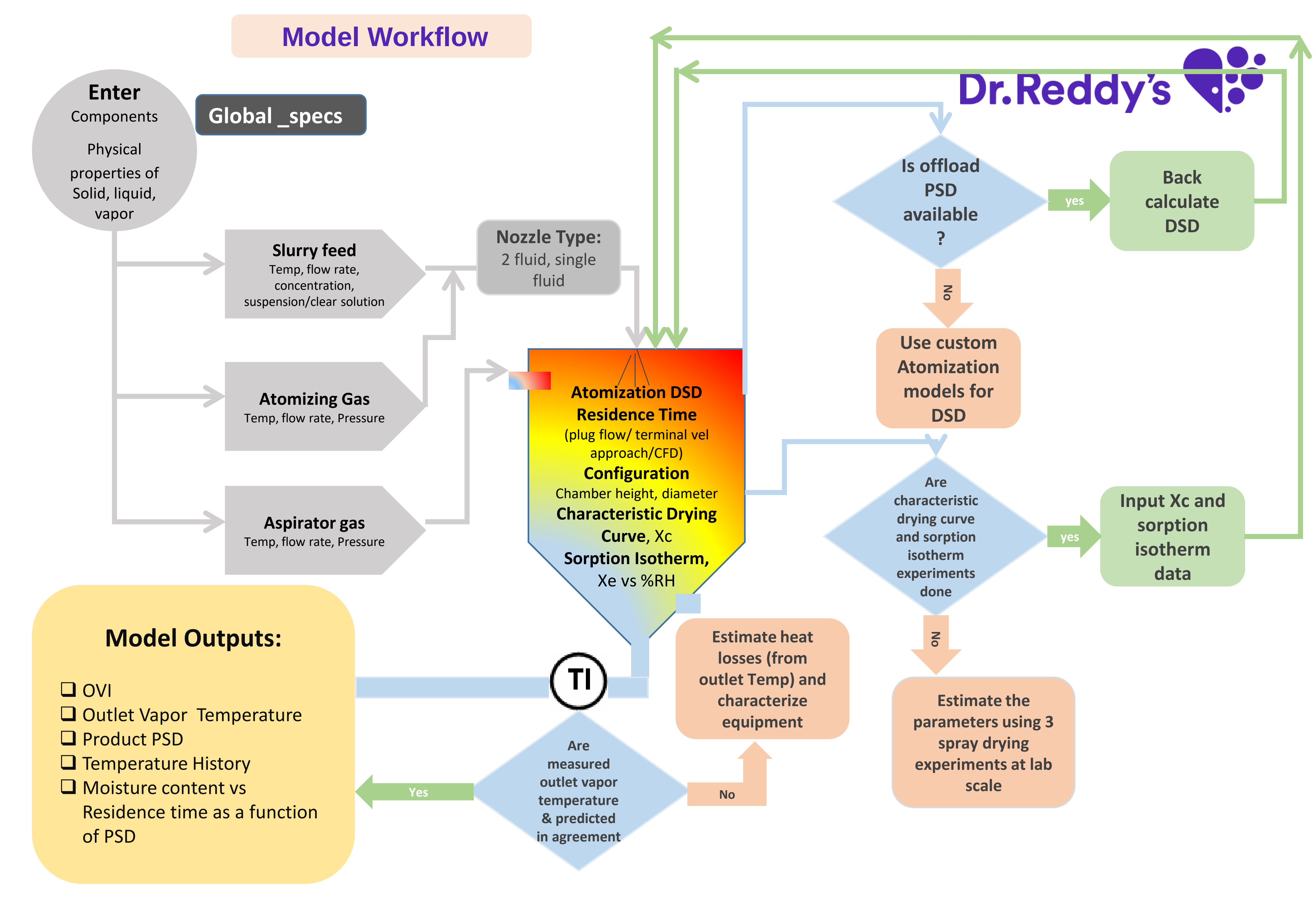
System Characterization
- Experimental /Operating conditions
- Equipment specifications
- Droplet size distribution from atomizer
- Droplet residence time
- Heat Loss

Equilibrium and drying properties
- Sorption isotherm
- Characteristic drying curve (including critical moisture content)
- Antoine vapour pressure coefficients
- Psychrometric ratio

gSOLIDS Model

Outputs

- OVI
- Outlet vapor temperature
- Outlet vapor humidity
- Droplet moisture content in spray dryer (all sizes) vs residence time
- Droplet temperature in spray dryer (all sizes) vs residence time
- Outlet PSD
  - Spray dryer outlet
  - Cyclone oversize
  - Cyclone undersize
- Droplet diameter in spray dryer (all sizes) vs residence time



Model Workflow
Dr.Reddy's
Enter
Components
Physical properties of Solid, liquid, vapor
Global _specs
Slurry feed
Temp, flow rate, concentration, suspension/clear solution
Atomizing Gas
Temp, flow rate, Pressure
Aspirator gas
Temp, flow rate, Pressure
Nozzle Type:
2 fluid, single fluid
Atomization DSD
Residence Time
(plug flow/ terminal vel approach/CFD)
Configuration
Chamber height, diameter
Characteristic Drying Curve, Xc
Sorption Isotherm,
Xe vs %RH
Is offload PSD available ?
yes
Back calculate DSD
No
Use custom Atomization models for DSD
Are characteristic drying curve and sorption isotherm experiments done
yes
Input Xc and sorption isotherm data
No
Estimate the parameters using 3 spray drying experiments at lab scale
TI
Estimate heat losses (from outlet Temp) and characterize equipment
Are measured outlet vapor temperature & predicted in agreement
Yes
No
Model Outputs:
❑ OVI
❑ Outlet Vapor Temperature
❑ Product PSD
❑ Temperature History
❑ Moisture content vs Residence time as a function of PSD

OUTLINE

Dr.Reddy's

1

- **Introduction**
  - **Spray Drying General aspects**
  - **Typical Challenges in industry**
  - **Need for a Mechanistic model**

2

- **gSOLIDS Spray Drying Model**
  - **Overview**
  - **Workflow**

3

- **Customization Aspects**
  - **Atomization models**
  - **Cyclone model**

4

- **Case Studies**
  - **Product 1**
  - **Product 2**

5

- **Conclusion**

Atomization Models

customized models added at flowsheet level

How do droplets form ?

There are different mechanisms due to which droplets form :

- High pressure drop
- Diffences in velocities
- Centrifugal force

Single fluid/ pressure nozzle

$$D_{3,2} = 286[(2.54 \times 10^{-2})D + 0.17]\exp\left[\frac{39}{v_{AX}} - (3.13 \times 10^{-3})v_1\right] \quad (10.10)$$

Two fluid/ pneumatic nozzle

$$D_{3,2} = \frac{535 \times 10^3\sqrt{\sigma}}{v_{REL}\sqrt{\rho}} + 597\left(\frac{\mu}{\sqrt{\sigma\rho}}\right)^{0.45} \times \left(\frac{1000\dot{V}_{FL}}{\dot{V}_{AIR}}\right) \quad (10.14)$$

Rotary Atomizer

$$D_{3,2} = 0.241\left(\frac{1}{N}\right)^{0.6}\left(\frac{1}{\rho}\right)^{0.3}\left(\frac{\mu\dot{M}}{2r\rho}\right)\left(\frac{\sigma}{N_v b}\right)^{0.1} \quad (10.7)$$

Ref: Handbook of industrial drying, Arun S Mujumdar)

Cyclone Model
customized model added to gSOLIDS standard libraries

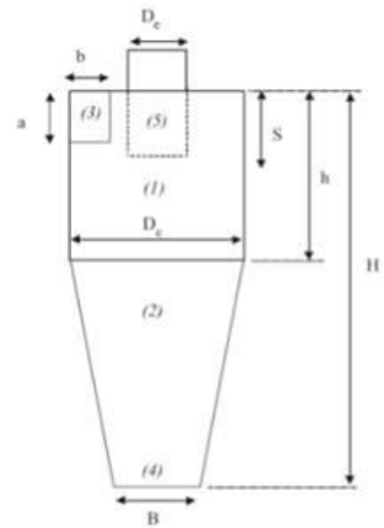
Lappel Cut diameter

According to this, cut diameter (dpc) is the size of the particles collected with 50% efficiency and is given as,

$$dpc = \left(\frac{9*\mu*Bc}{2*\pi*Nc*vi*(\rho p-\rho)}\right)^{0.5}$$

μ = viscosity (Pa.s)
Bc = inlet width (m)
vi = inlet gas velocity (m/s)
ρp = particle density (kg/m^3)
Nc = number of turns

$$Nc = \frac{h + \frac{H-h}{2}}{a}$$



The collection efficiency (E) as a function of the ratio of particle diameter to cut diameter can be obtained by:

$$E = \frac{1}{1 + \left(\frac{dpc}{dp}\right)^2}$$

Ref: NPTEL – Chemical Engineering Design – II, General Design Consideration of Cyclone Separator.

OUTLINE

1
- **Introduction**
  - **Spray Drying General aspects**
  - **Typical Challenges in industry**
  - **Need for a Mechanistic model**

2
- **gSOLIDS Spray Drying Model**
  - **Overview**
  - **Workflow**

3
- **Customization Aspects**
  - **Atomization models**
  - **Cyclone model**

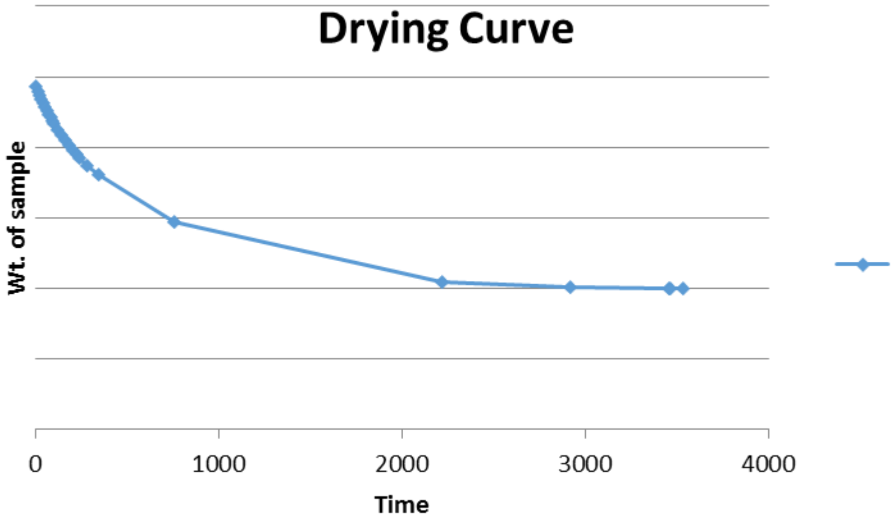
4
- **Case Studies**
  - **Product 1**
  - **Product 2**

5
- **Conclusion**

Product 1

Parameters obtained at Lab Scale

Dr.Reddy's

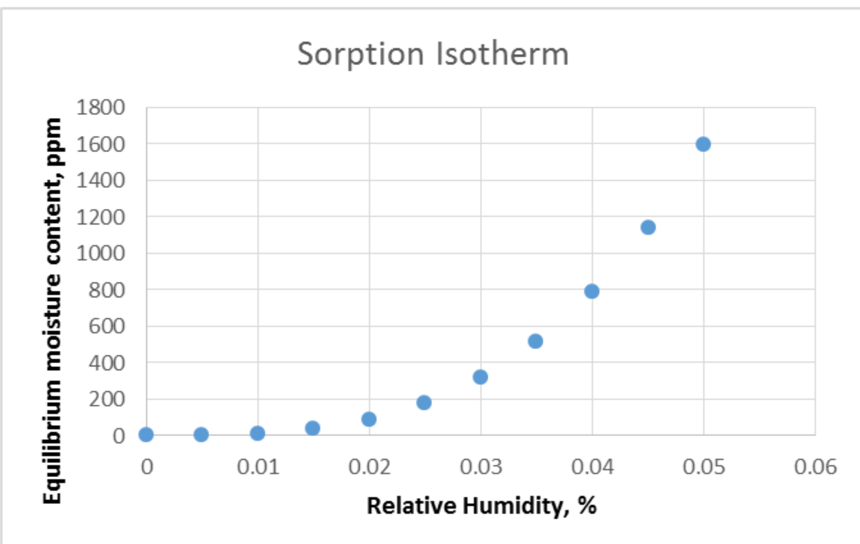


Critical Moisture content , Xc

Obtained from an independent experiment performed in TGA(Thermo gravimetric Analyzer)

Sorption isotherm , % RH = Constant * (Xeq) ^Power

Obtained from parameter estimation in gSOLIDS using the following experiments

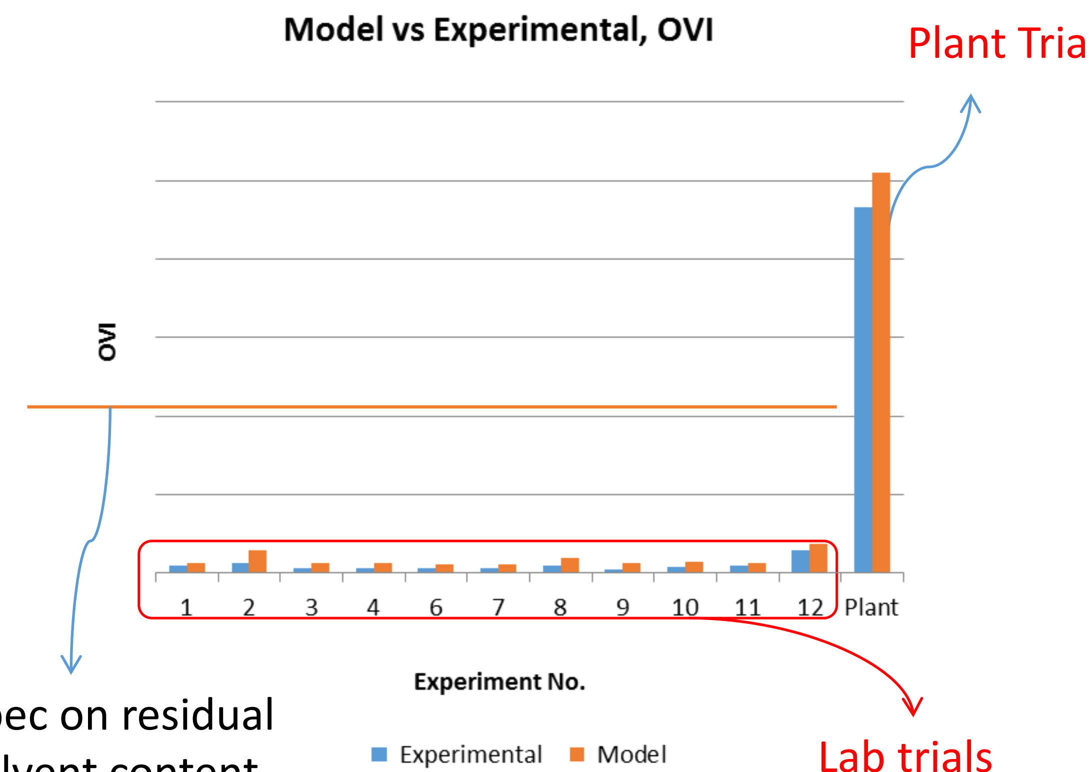


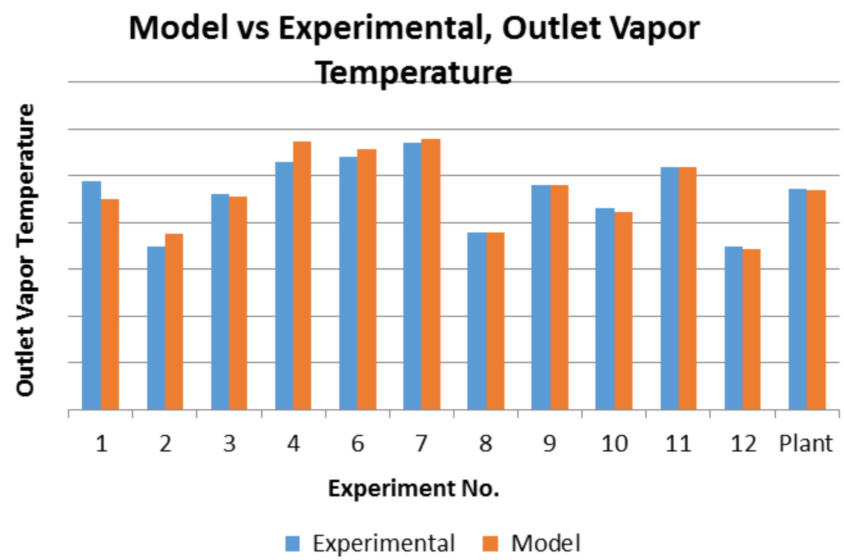
Estimate_sorption

Experiment	Include in estimation
DoE_Experiment1	☑
DoE_Experiment_cp	☑
Pre_DOE	☑

These are scale independent parameters characteristic of API and used for prediction at plant scale

Model Validation





Model and experimental data seem to be well in agreement in most of the cases

Operating conditions at which the OVI can further be reduced at plant explored using gSOLIDS model and recommendations given .

Comparison between 2fluid and single fluid nozzle trials at the recommended operating conditions using gSOLIDS simulations

Key Outputs (Trial with 2fl nozzle)

Variable	Value	Unit
OVI_solvent 1	680	ppm
Outlet Vapor temperature	44.4	C
PSD , d10	11	µm
PSD , d50	15	µm
PSD, d90	20	µm
Cyclone Yield (Theoretical)	85.4	%

Key Outputs (Trial with single fluid nozzle)

Variable	Value	Unit
OVI_solvent 1	1250	ppm
Outlet Vapor temperature	46	C
PSD , d10	21	µm
PSD , d50	28	µm
PSD, d90	33	µm
Cyclone Yield (Theoretical)	95	%

Higher yield loss due to collection of fines in the Bag Filter

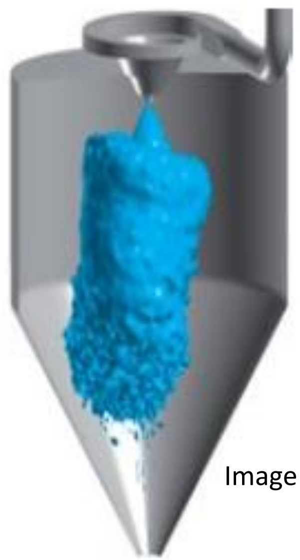
Note: Cyclone yield does not account for wall deposits and equipment fouling.

Cyclone Yield

Model vs Actual….

Cyclone model does not take into account losses due to wall deposits (including equipment fouling due to poor product properties) in spray chamber as well as cyclone.

What model assumes….



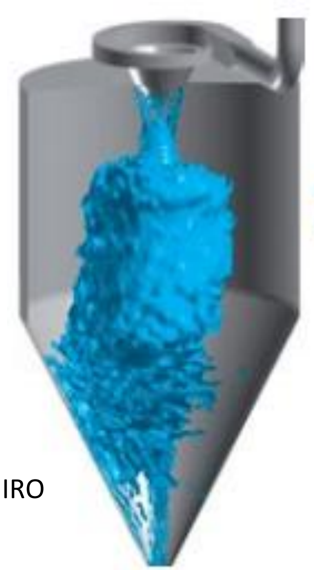


Image Courtesy: GEA NIRO

What actually happens….

To address wall deposits due to semi dried particles hitting the walls and getting stuck, more advanced simulations like CFD simulations are needed.

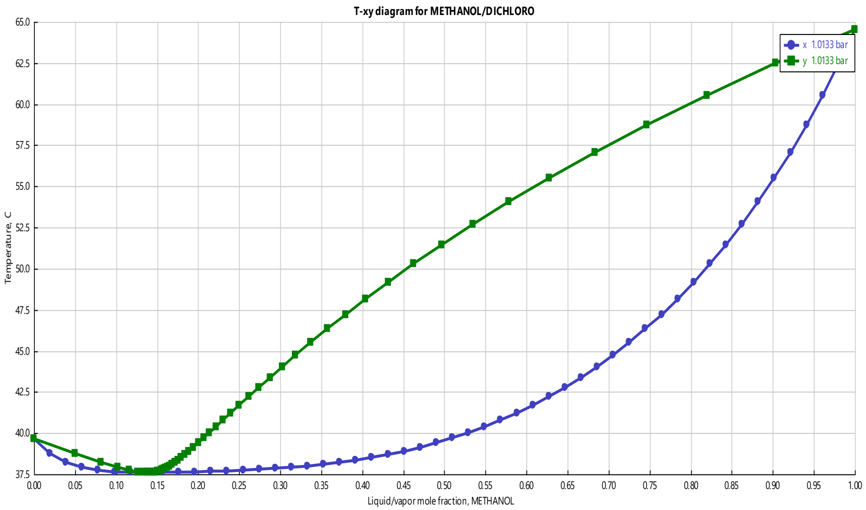
Ref: J Sloth – Method for improving spray drying product equipment and product properties, Interceram 03–04/2010, Pg 193-197.

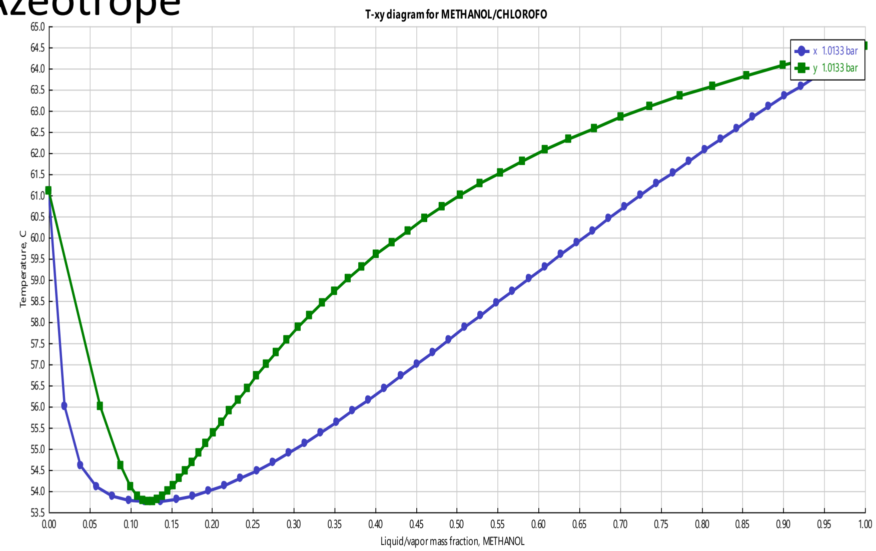
Product 2

T-xy diagram for mixtures with complex VLE

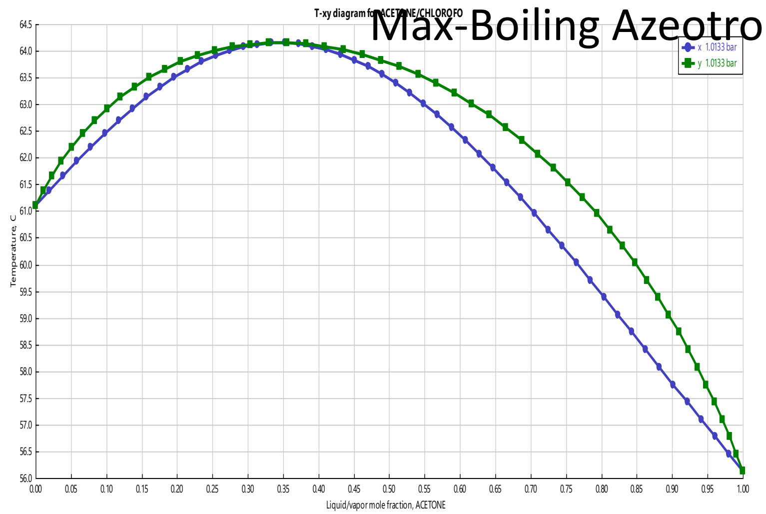
How will the presence of an azeotrope affect spray drying process ?…….

Min-Boiling Azeotrope





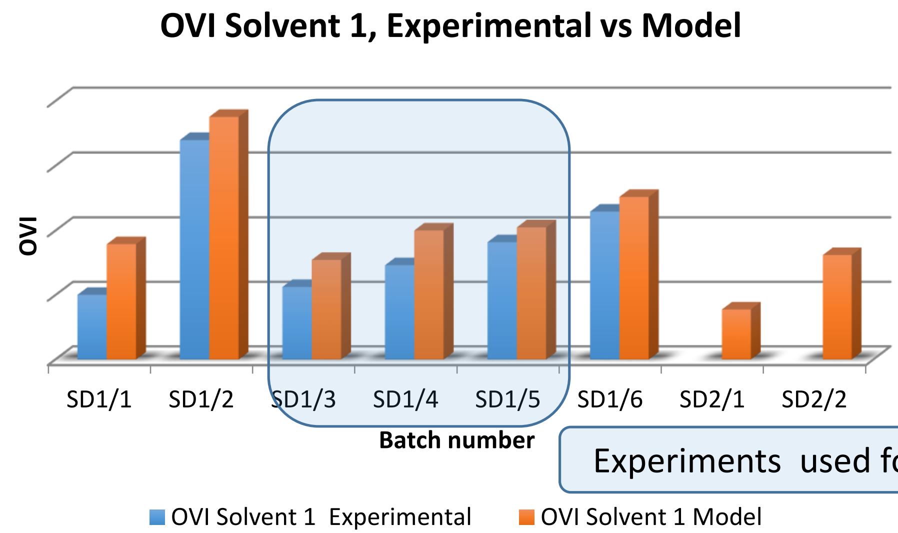
Max-Boiling Azeotrope

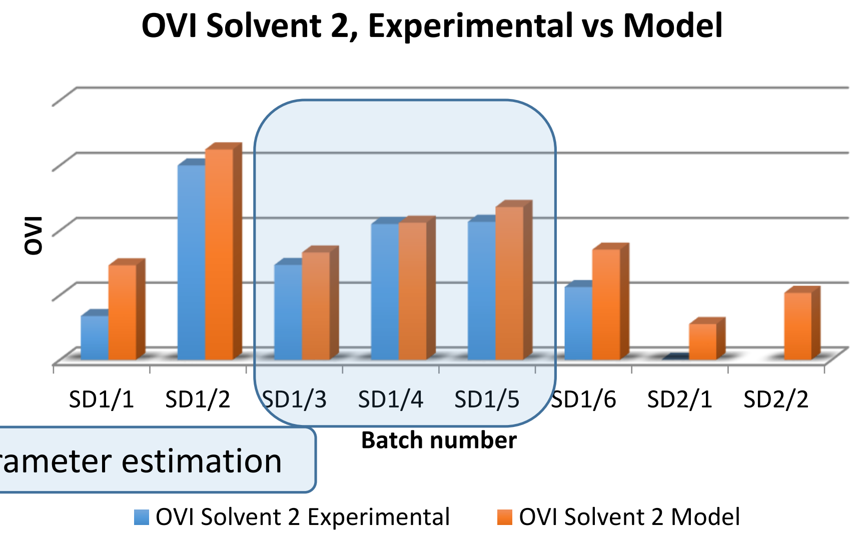


Handling multicomponent drying with complex VLE in gSOLIDS

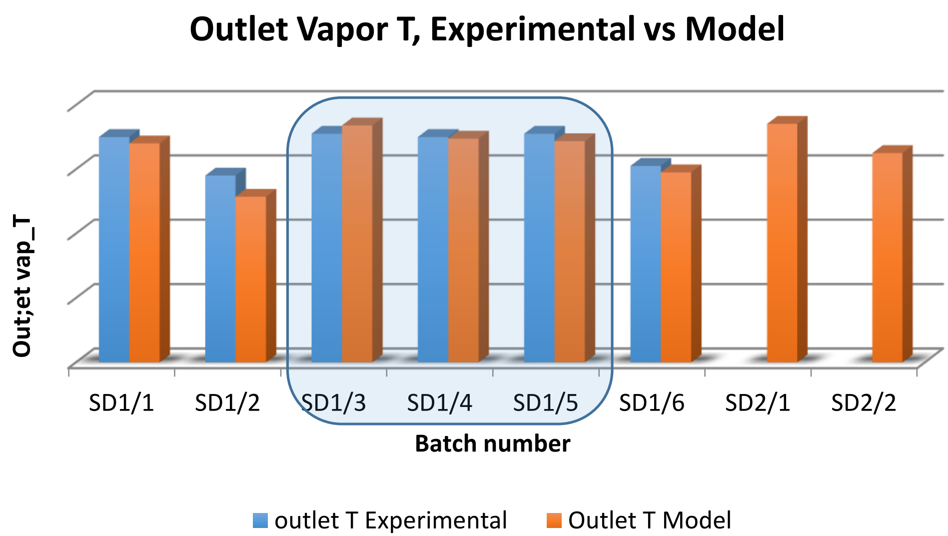
Product 2

Spray dryer 1 and Spray dryer 2 (transition from from closed loop to open loop)





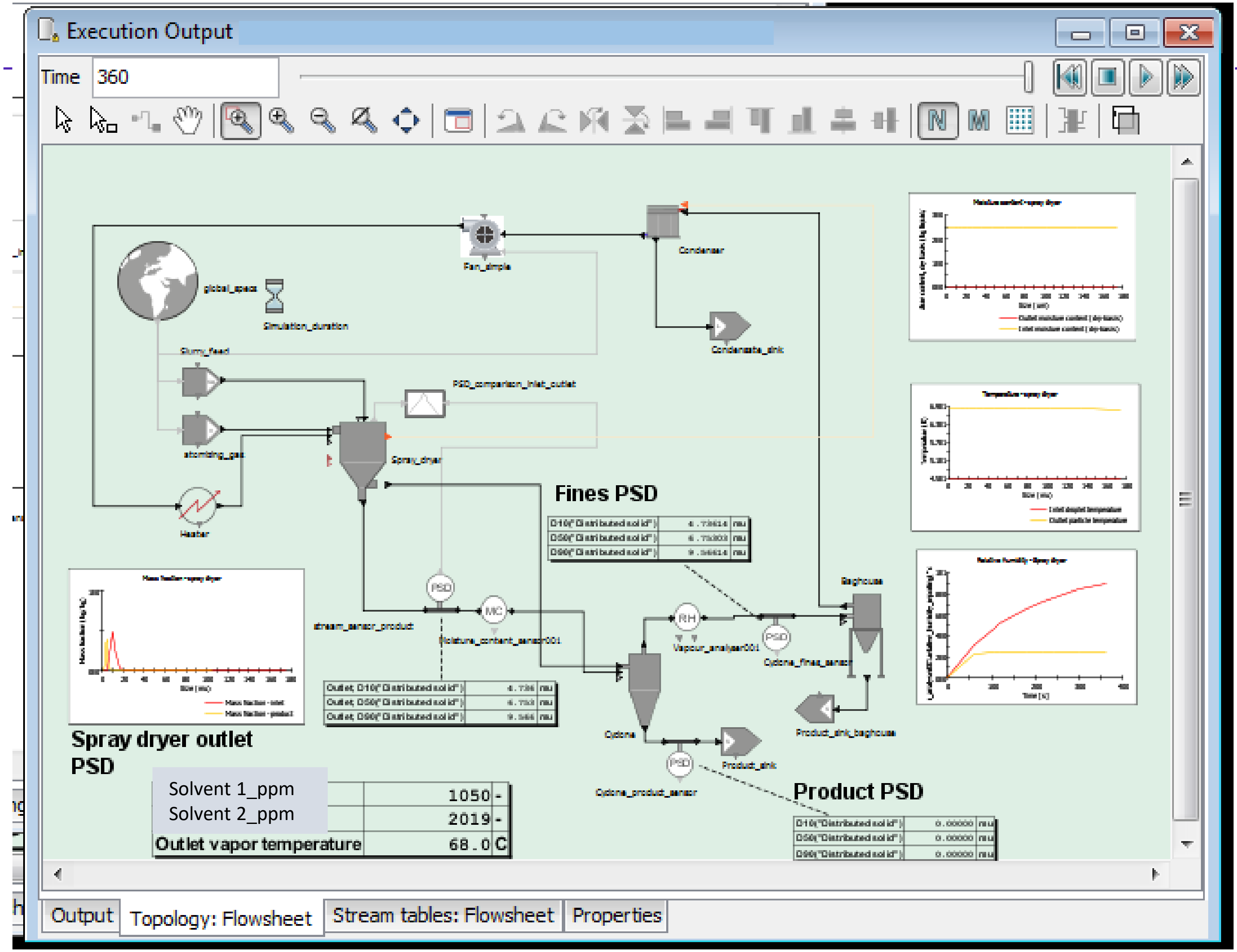
Experiments used for parameter estimation



Features Implemented

- gSOLIDS standard Libraries
- Customized Atomization models
- Multiflash for physical properties
- Customized cyclone model
- Customized Closed loop operation
- Integration of all the unit operations involved in spray drying process

Screenshots of gSOLIDS Model Output (closed loop)



Model gives the relative humidity build up at the spray dryer outlet over time

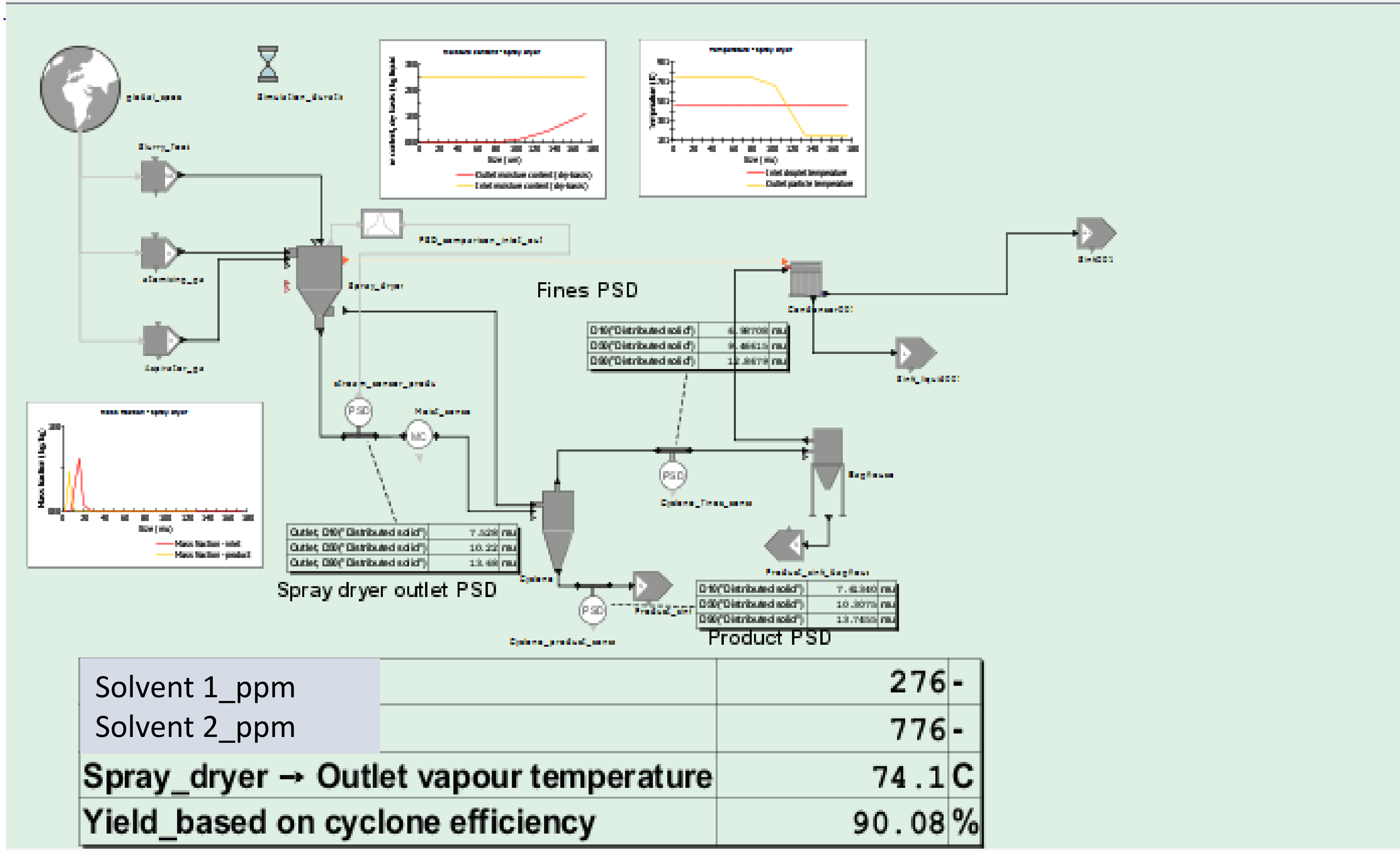
RH vs time plot in combination with the sorption isotherm can be used to find out the maximum time for the closed loop operation

Multicomponent droplet evaporation and drying behaviour can be simulated

Phase equilibrium properties (SLE, SLLE,VLLE, etc) are taken into consideration

All the unit operations in spray drying process are put together in one flowsheet to understand the effect of different CPPs on the CQAs

Screenshots of gSOLIDS Model Output (Open loop)



OUTLINE

Dr.Reddy's

1
- **Introduction**
  - **Spray Drying General aspects**
  - **Typical Challenges in industry**
  - **Need for a Mechanistic model**

2
- **gSOLIDS Spray Drying Model**
  - **Overview**
  - **Workflow**

3
- **Customization Aspects**
  - **Atomization models**
  - **Cyclone model**

4
- **Case Studies**
  - **Product 1**
  - **Product 2**

5
- **Conclusion**

Concluding Remarks

- Atomization models are over predicting the initial drop size.
- Back calculating DSD using offload PSD measurement gave more accurate results.
- Estimated residence times from known spray drying experiments are less than the mean gas residence time.
- Integrating all unit operations involved in spray drying process in one flowsheet gave much better understanding into the process.

Future Work

- Predicting equipment fouling and wall deposits using CFD simulations and estimate the yield loss .
- Inclusion of a better atomization model that would give the DSD as an output from the model.
- Implementation of multizonal CFD models.

Acknowledgements

Team at Dr.Reddys

- Y. Sesha Reddy
- Neha Palagiri
- Suresh Kumar Karra
- Mohammed Yakoob Sardar
- S Siva Naga Raju
- Raymon Krul
- Ravi Chandra Palaparthi
- Srividya Ramakrishnan
- Sudarshan Mahapatra

Management at DRL

PSE Support

Deon Pistorius

David Slade

Hassan Mumtaz

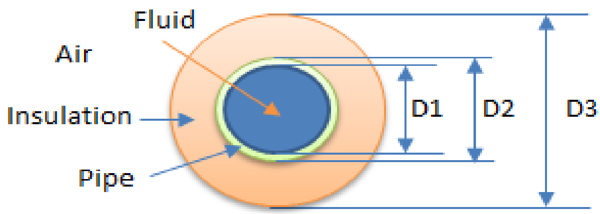
Sean Birmingham

Thank You

Back UP

Heat Loss Calculation

Wall-environment heat loss from spray dryer is characterized from a dry gas run



$$U = \frac{1}{\frac{D_3}{D_1 . h_{in}} + \frac{D_3 . ln\left(\frac{D_2}{D_1}\right)}{2. k_{PIPE}} + \frac{D_3 . ln\left(\frac{D_3}{D_2}\right)}{2. k_{INSULATION}} + \frac{1}{h_{AIR}}}$$

Inputs needed

S.No	Item
1	Equipment dimensions
2	Equiment MoC
3	Type of Insulation and thickness
Inputs from Dry Gas Run	
4	Flow rate of dry gas
5	Outlet vapour temperature
6	Surface Temperature

Assumption:

Heat Transfer coefficient can be assumed to remain constant for a given range of operating temperatures, although in reality it varies, which is a fair assumption for a given temperature range.
Otherwise, it can be calculated based on the operating temperature, as and when needed.

Reference: Heat Loss from insulated pipe, Chemical engineer's Guide.

Fundamental differences between QBD and systems based pharmaceutics approach

	pre-QbD	"QbD 1.0"	"QbD 2.0"
Experiment design method	OFAT	Factorial design / Fractional factorial design	Mechanistic model-based
Aim of experimental programme	Attain improve-ments in the system	Determine combined effect of CPPs on CQAs Identify robust operating points / regions	Targeted at estimating parameters of physical model Use validated model to identify robust, optimal operating regions
Models used	Typically none	Statistical models (MVDA)	Advanced Process Modelling (APM): Mechanistic models
Limitations / challenges of the approach	Combined effect of changes in CPPs unknown, so difficult to predict robustness	Very resource intensive experimental programme Limited ability to transfer knowledge to other scales / equipment Regulatory acceptance / understanding	Selecting appropriate mechanistic model (model discrimination) Not widely applied yet → training and culture change required Regulatory acceptance / understanding

Ref: Presentation titiled SBP- A systems approach for design of robust drug products and their manufacturing processes t properties, Interceram 03–04/2010, Pg 193-197.

Atomization models – Key Equations and References

- **Drop size calculation for a pressure nozzle is given by,**

$$D_{3,2} = 286[(2.54 \times 10^{-2})D + 0.17]\exp\left[\frac{39}{v_{AX}} - (3.13 \times 10^{-3})v_1\right] \quad (10.10)$$

where the axial velocity v_{AX} (m/s) and the inlet velocity v_1 (m/s) are determined as follows:

$$v_{AX} = \frac{D_1^2}{2Db} v_1 \quad (10.11)$$

$$v_1 = \frac{\dot{V}_1}{A_1} \quad (10.12)$$

In this equation, D is orifice diameter (m), D_1 is inlet channel diameter (m), A_1 is inlet channel area (m^2), $\dot{V}_1$ is volumetric flow rate (m^3/s), and b is thickness of fluid film in the orifice. The resulting Sauter mean diameter is in μm.

Ref. Correlation for Pressure nozzle to calculate D3,2, Handbook of industrial drying, Arun S Mujumdar)

- **Drop size calculation for a two fluid nozzle is given by,**

$$D_{3,2} = \frac{535 \times 10^3 \sqrt{\sigma}}{v_{REL}\sqrt{\rho}} + 597\left(\frac{\mu}{\sqrt{\sigma\rho}}\right)^{0.45} \times \left(\frac{1000\dot{V}_{FL}}{\dot{V}_{AIR}}\right) \quad (10.14)$$

where σ, ρ, and μ are the fluid surface tension (N/m), density (kg/m^3), and viscosity (Pa s), respectively, and $\dot{V}_{FL}$ and $\dot{V}_{AIR}$ are volumetric flow rates of fluid and air (m^3/s), respectively. Instead of relative velocity v_{REL} (m/s), the outlet velocity of air may also be substituted.

Ref. Correlation for two fluid nozzle to calculate D3,2, Handbook of industrial drying, Arun S Mujumdar)