FORMULATION DISPERSION STABILITY SYMPOSIUM

Turbiscan, an easy and efficient way for physical stability measurement

Pascal Da Costa – October 19th 2021

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Formulaction
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STABILITY & SIZE
MICRORHEOLOGY
RHEOLOGY ON CHIP

Formulaction

Company Overview

- Formulaction (Toulouse, FR) is a leader in stability and microrheology measurements.
  - ✓ Company created in 1994
  - ✓ 3 ranges of products: Turbiscan, Fluidicam & Rheolaser
  - ✓ Direct office in the USA (Columbus, OH) , Germany & distribution : + 40 countries
  - ✓ Over 2,500 instruments, Over 2300 publications, 200+ patents

- Formulaction mission : Provide characterization tool to the formulators in cosmetics, food, pharmaceuticals, oil & petroleum, chemicals, paint & ink, electronics....

Formulaction
Smart scientific analysis

FORMULATION

« overall know-how to develop and manufacture products with desired properties as stated by the specifications »

PHYSCIAL STABILITY
Introduction

What is a liquid dispersion ?

Cosmetic





Food & Beverage







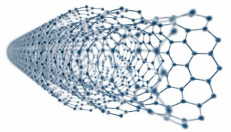
Ink & Paint

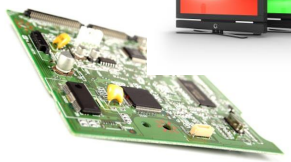





Pharmaceutical

Materials….

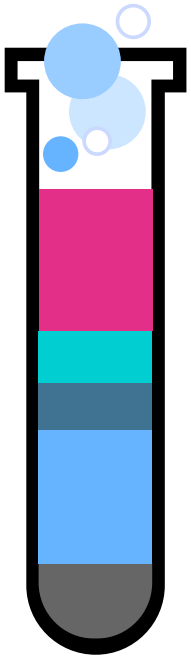

Oil & Petroleum

PHYSCIAL STABILITY
Introduction

What is a liquid dispersion ?

A mixture

Multiple ingredients, non miscible phases (dispersed phase and continuous phase)



Different types

- Liquid/liquid = emulsion
- Solid/liquid = suspension
- Gas/liquid = foam

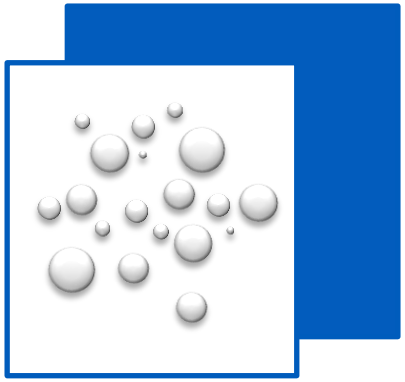
Stable/Unstable

For user appreciation, the formulation must remain stable

PHYSICAL STABILITY
Definitions

- What is considered a Stable formulation ?

Initial state



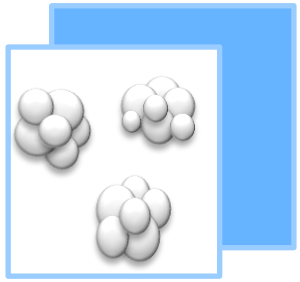
In practice, no such product exist

Every system evolves

Phyiscal unstability phenomena

Particle size increase

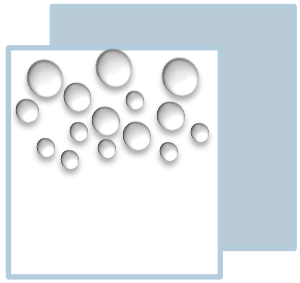
Flocculation



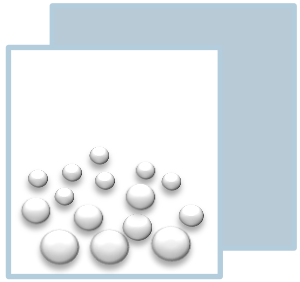
Coalescence

Migration phenomena

Creaming



Sedimentation



PHYSICAL STABILITY
Classical tests

⇒ Classical method for stability determination

BOTTLE TEST

- Direct Method
- Inexpensive
- Corresponds to real conditions (no stress…)

But What if the change is not easily visible ??

Limitations of the bottle test:

- Not sensitive -> may require several months and high temperatures
- Only sensitive to particle migration
- Not Objective : Depends on the Operator
- Doesn't quantify the phenomena

Before

After

PHYSICAL STABILITY
Turbiscan®

What is the alternative ?

MULTIPLE LIGHT SCATTERING

TURBISCAN®

Analyses migration destabilization phenomena

AND

Size variation on samples with particle size from 10nm to 1mm at concentrations from 10^{-4}% to 95% v/v

Analyze the sample AS IT IS!

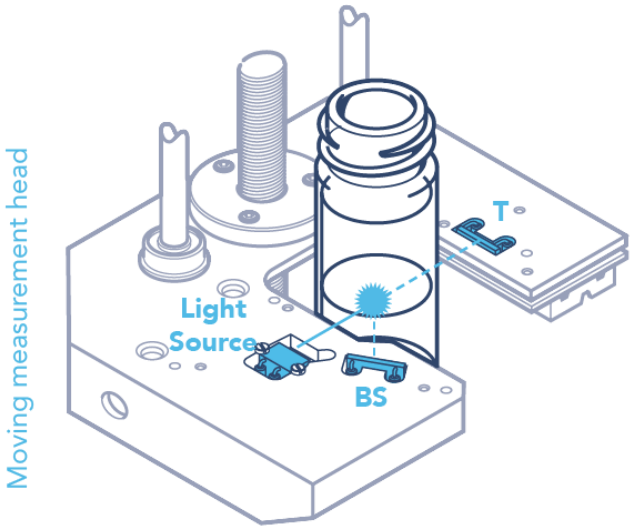
No dilution, no stress, no probes
Same conditions as visual tests
Only faster and more precisely

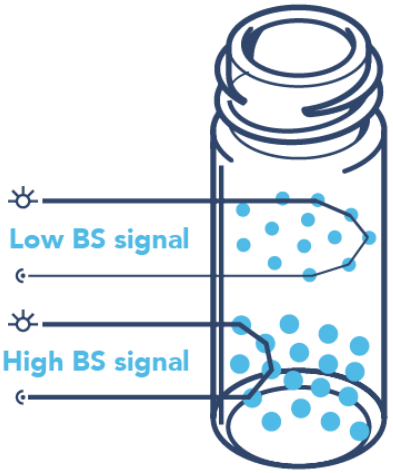
PHYSICAL STABILITY

Turbiscan®

TURBISCAN TECHNOLOGY

How does it work?





Backscattering and Transmission signals depend on :

d : <u>Particle size</u> & Φ : <u>Particle concentration</u>

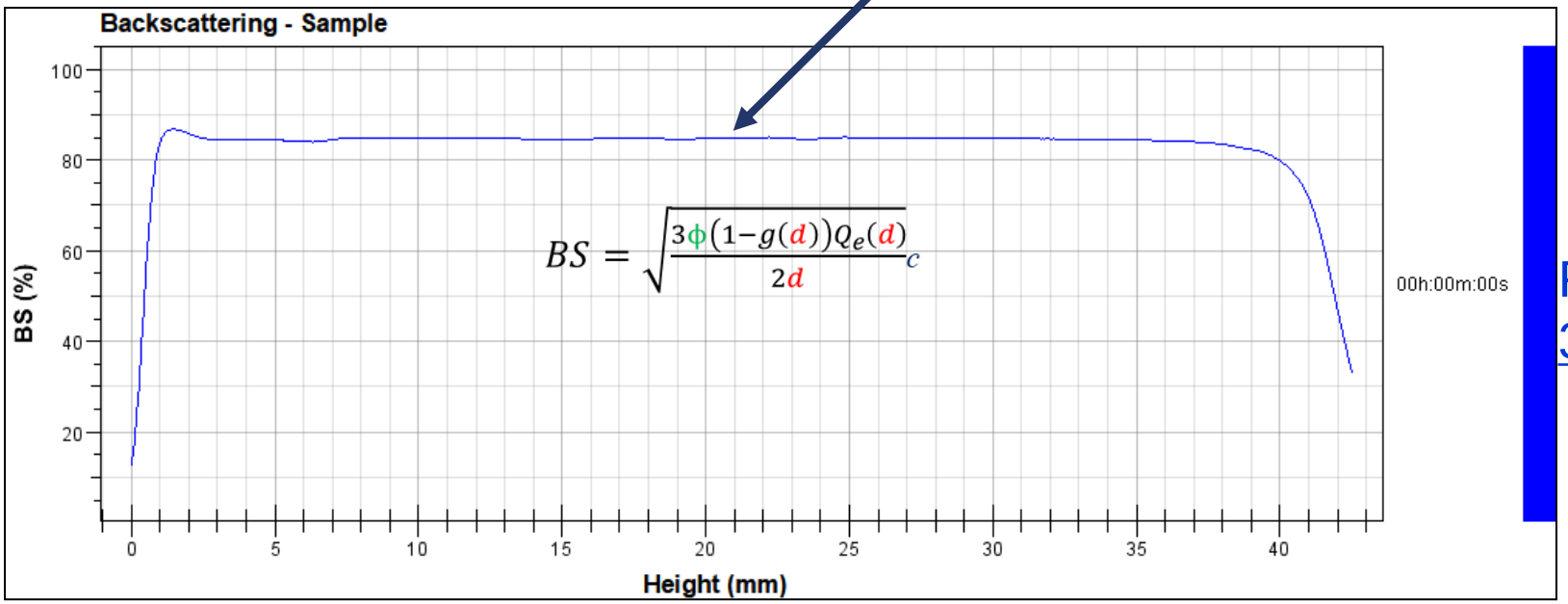
Scan are made **all over the sample height** and **periodically**

Signal variation ➡ Variation in the sample ➡ Monitoring of stability

TURBISCAN TECHNOLOGY

How does it work?

Particle size can be determined from the single curve

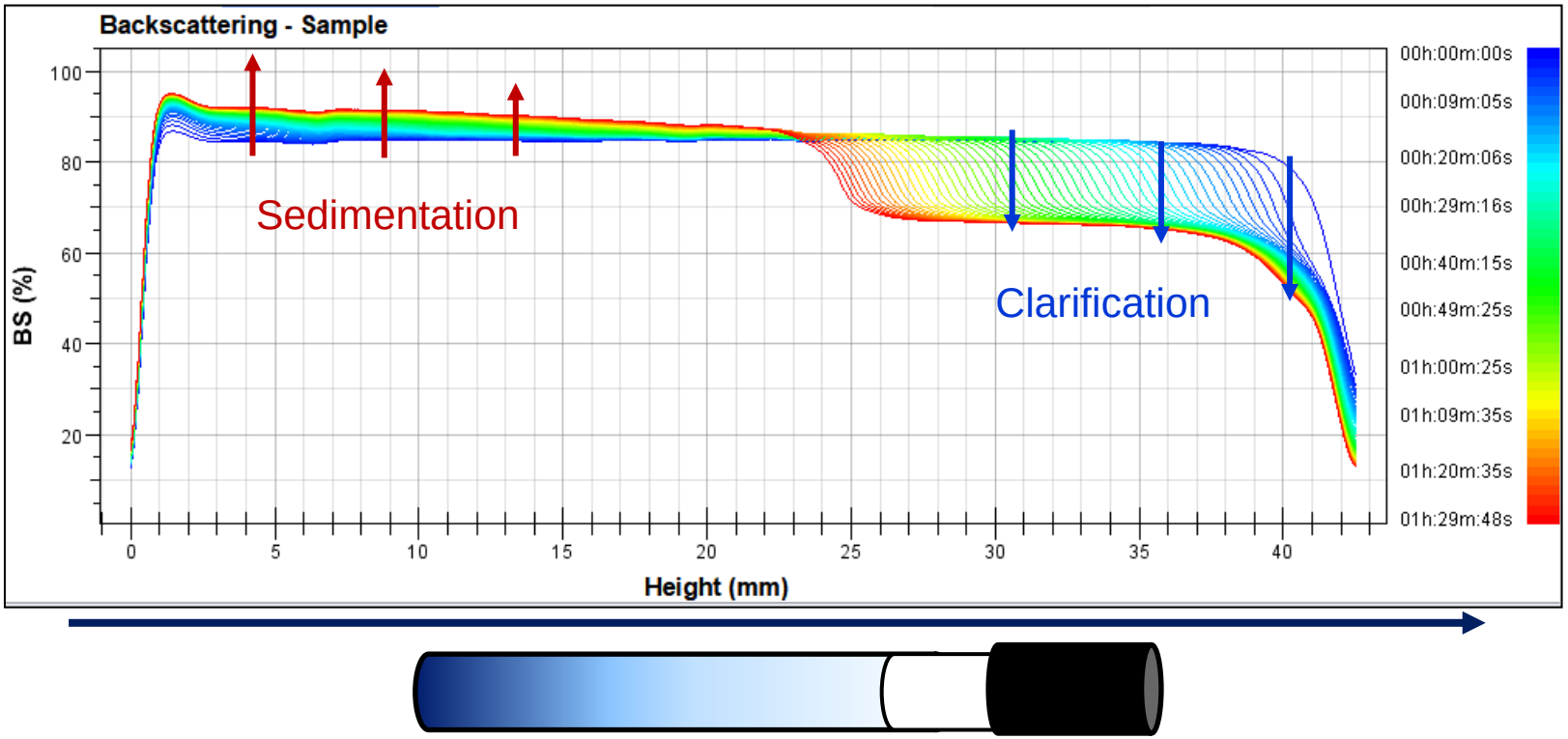


First scan
30 seconds

Single scan = **Size**

TURBISCAN TECHNOLOGY

How does it work?



Multiple scans = time

Multiple scans, if variation = **DESTABILIZATION**

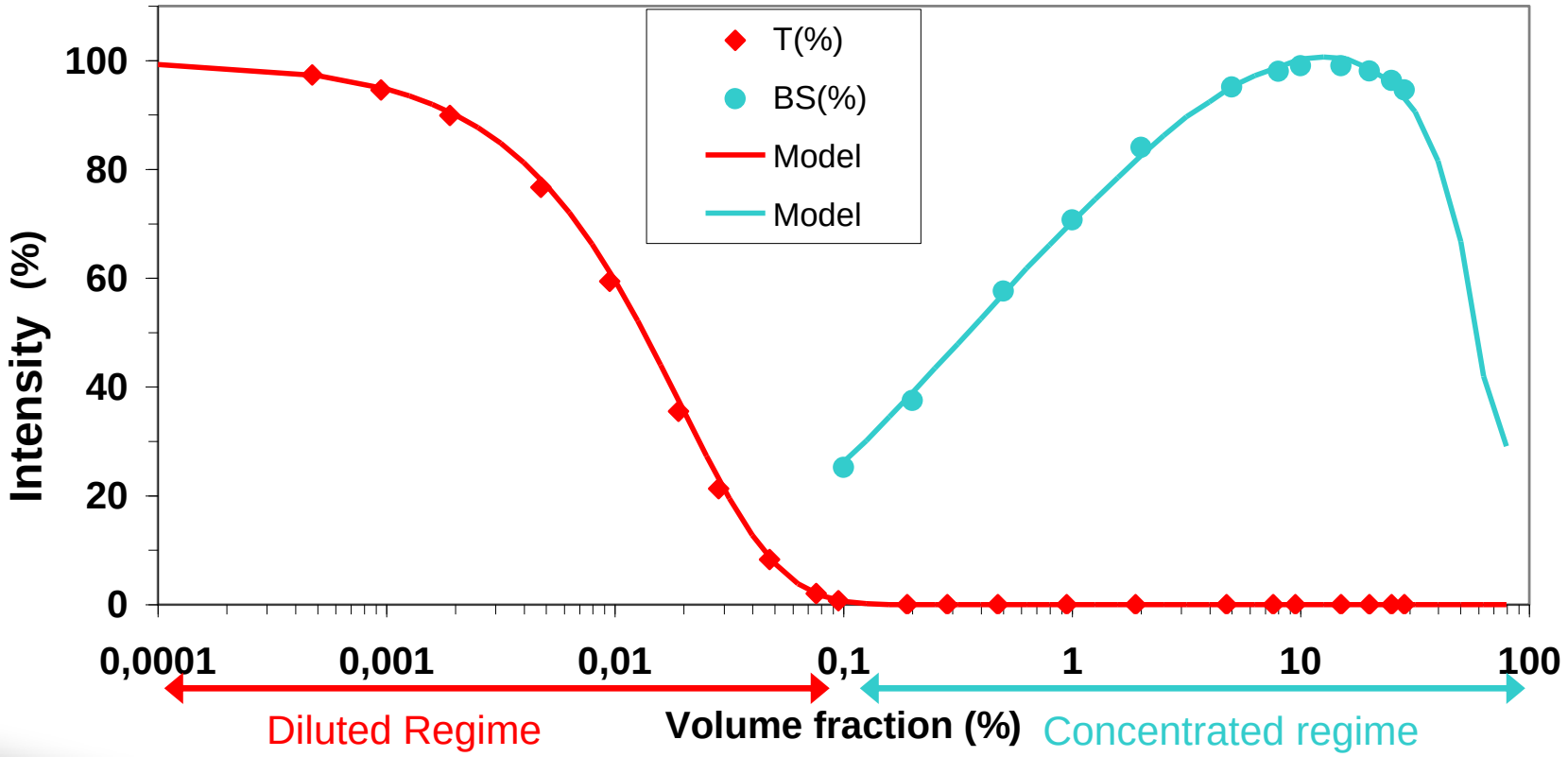
TURBISCAN TECHNOLOGY

How does it work?

Variation of particle concentration

ESTAPOR latex suspension (polystyrene in water)

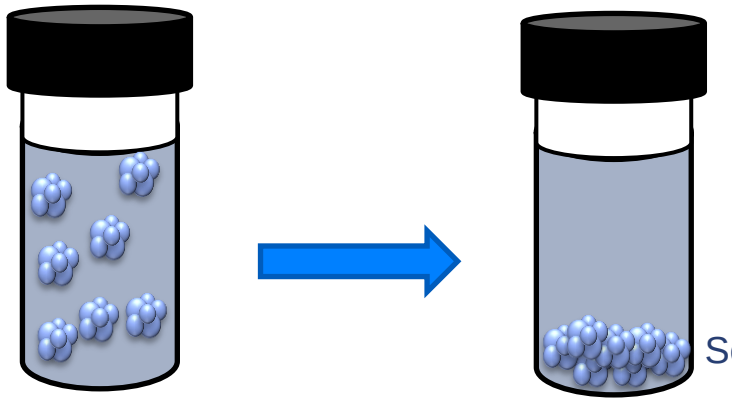
d = 0.3µm, np = 1.59, nf = 1.33, Wavelenght = 880nm



Concentration range : from 0,001 to 95%

TURBISCAN TECHNOLOGY

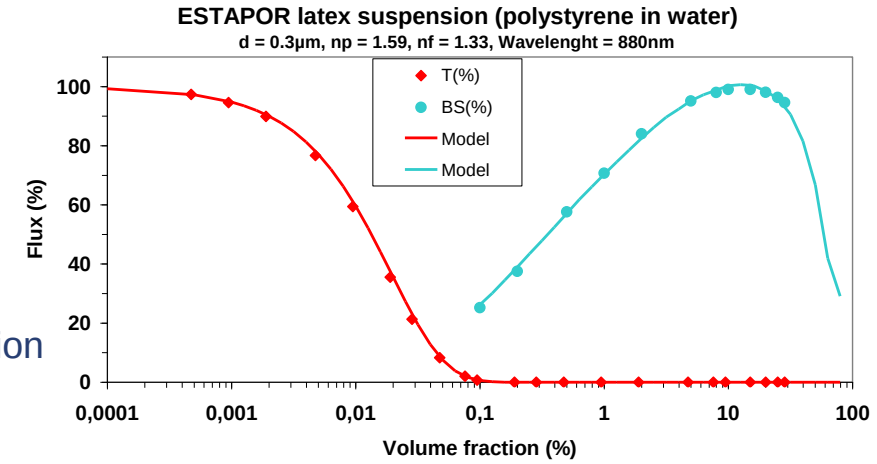
How does it work?

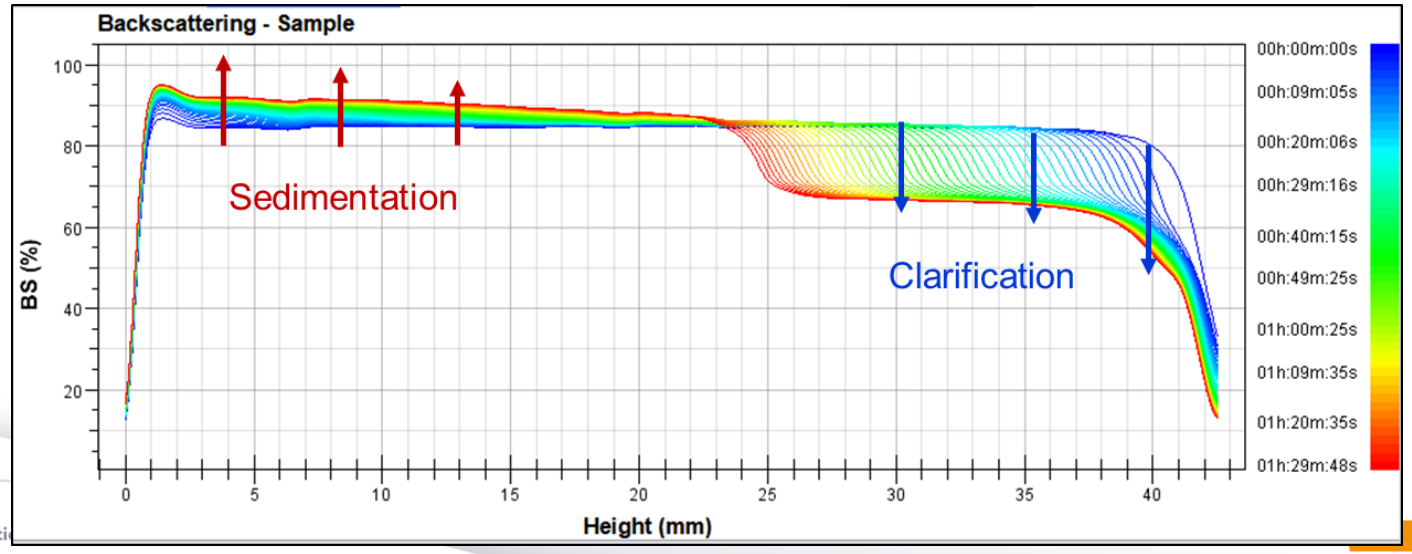


Opaque sample

Sedimentation

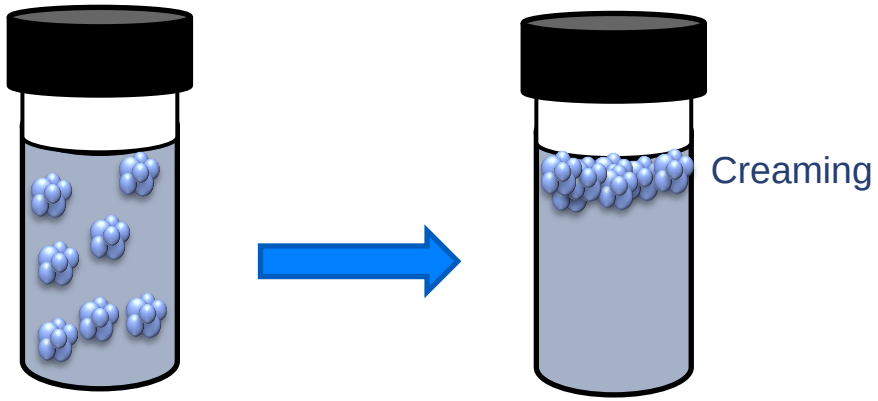
Increase in BS at the bottom
Decrease in BS at the top





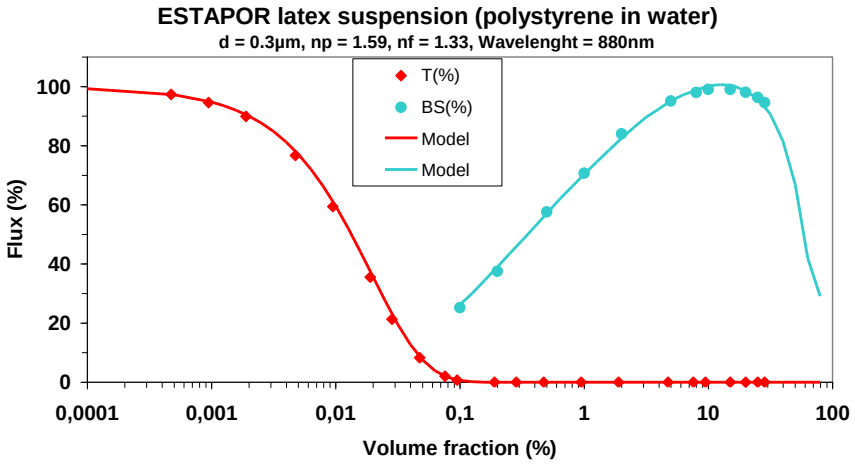
TURBISCAN TECHNOLOGY

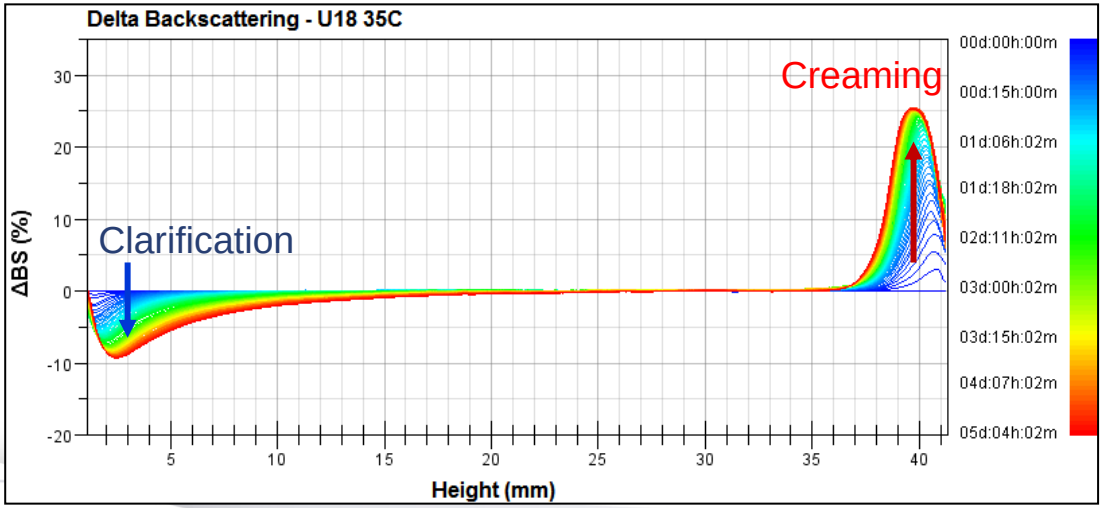
How does it work?



Opaque sample

Increase in BS at the top
Decrease in BS at the bottom



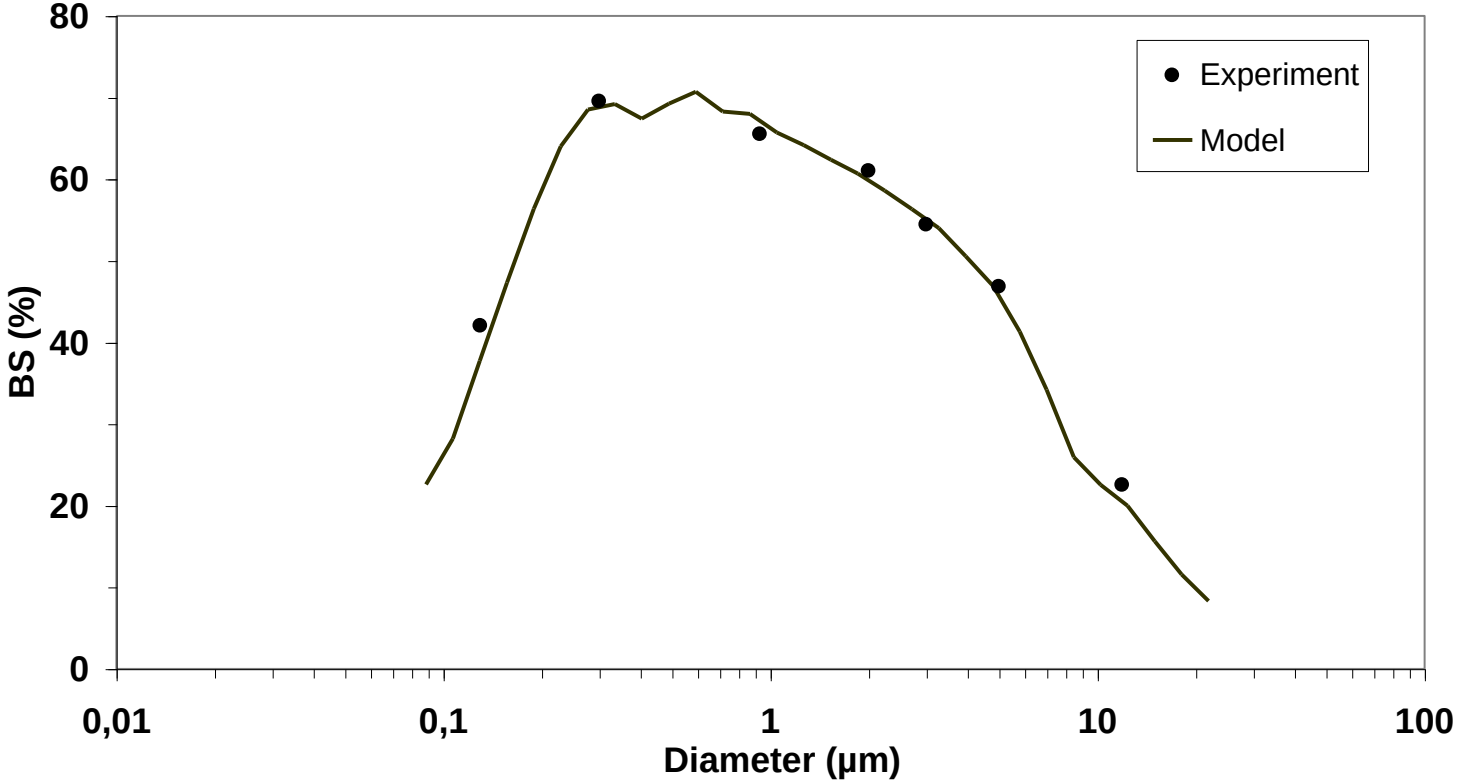


TURBISCAN TECHNOLOGY

How does it work?

Variation of Particle size

Latex suspensions from ESTAPOR (polystyrene in water)
ϕ = 1%, np = 1.59, nf = 1.33, Wavelength= 880nm

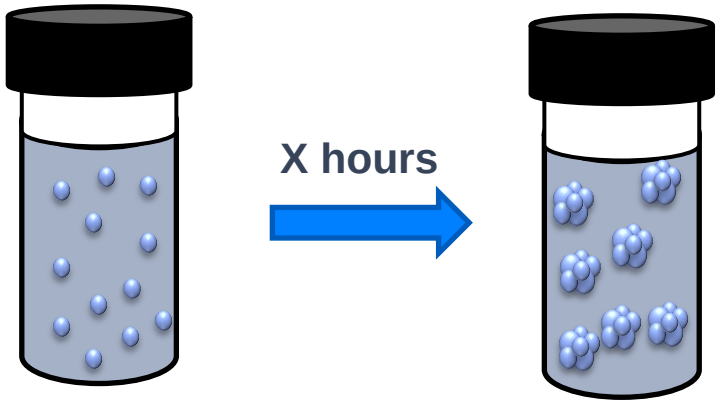


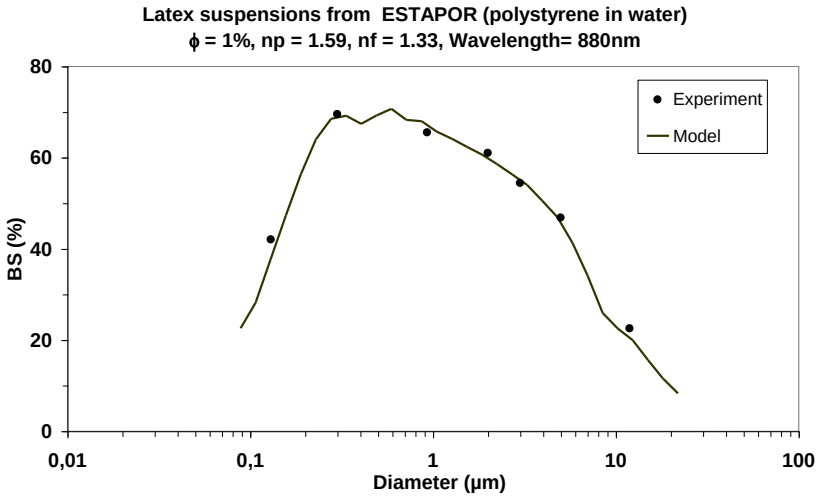
Size range : from 1nm to 1mm

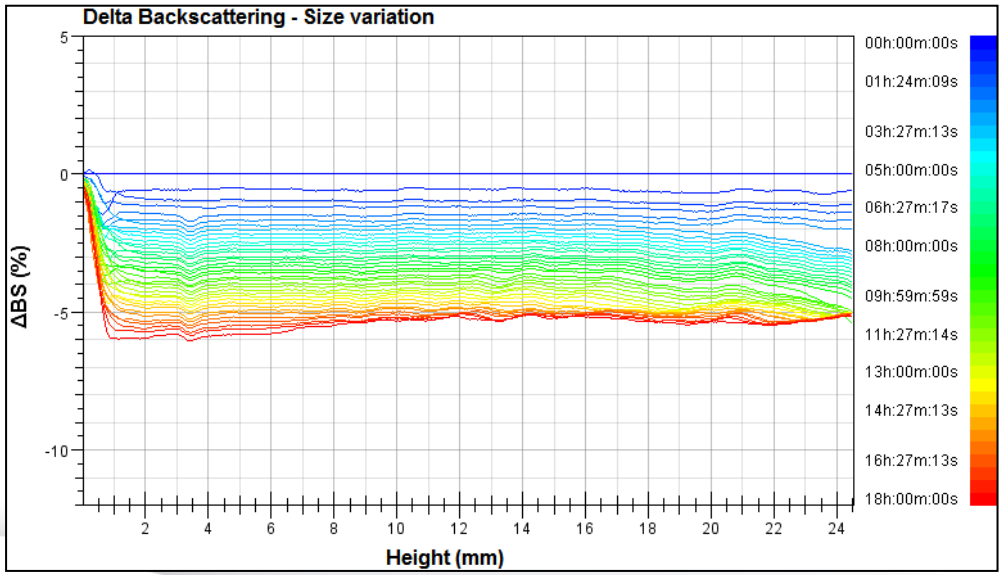
TURBISCAN TECHNOLOGY

How does it work?

Agglomeration of particles



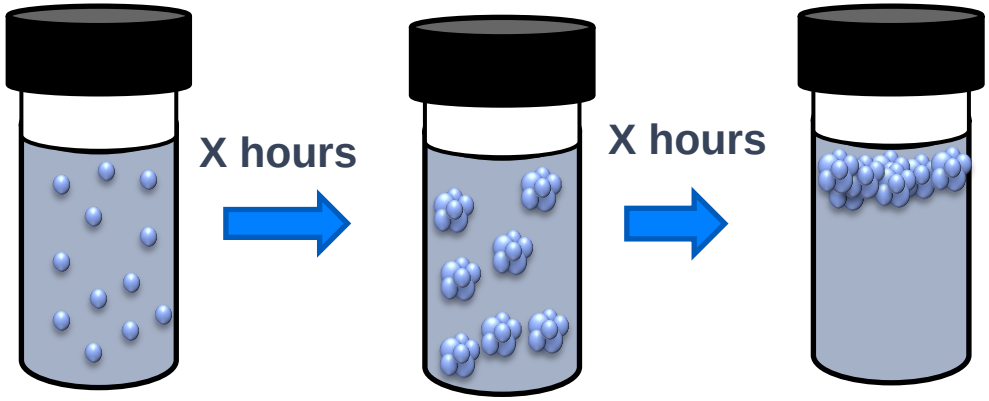


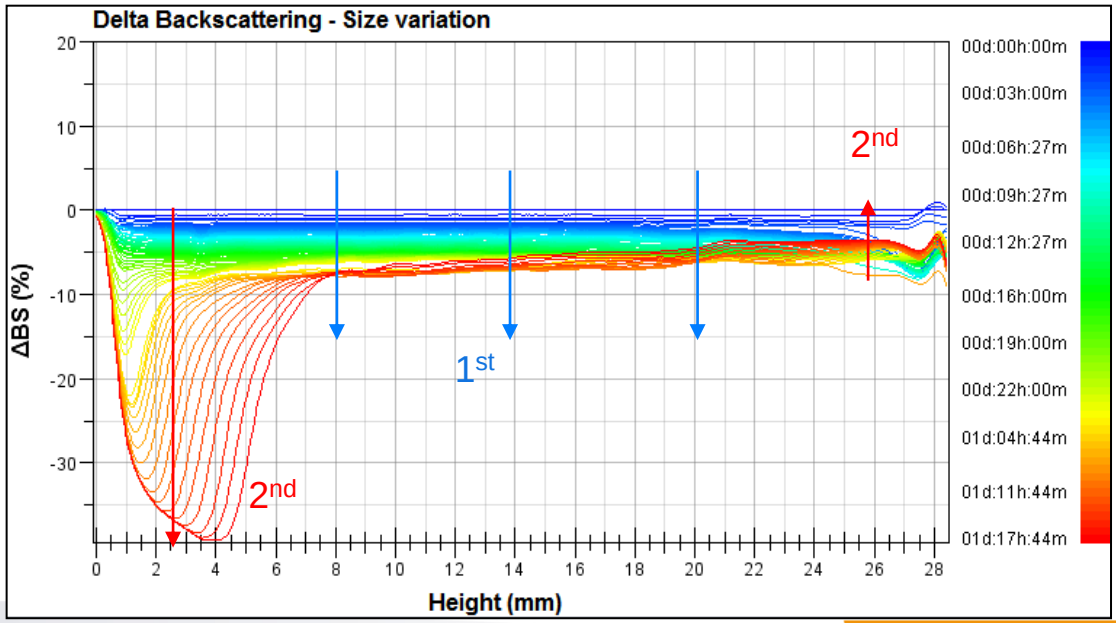


TURBISCAN TECHNOLOGY

How does it work?

Combination of size increase and particle migration





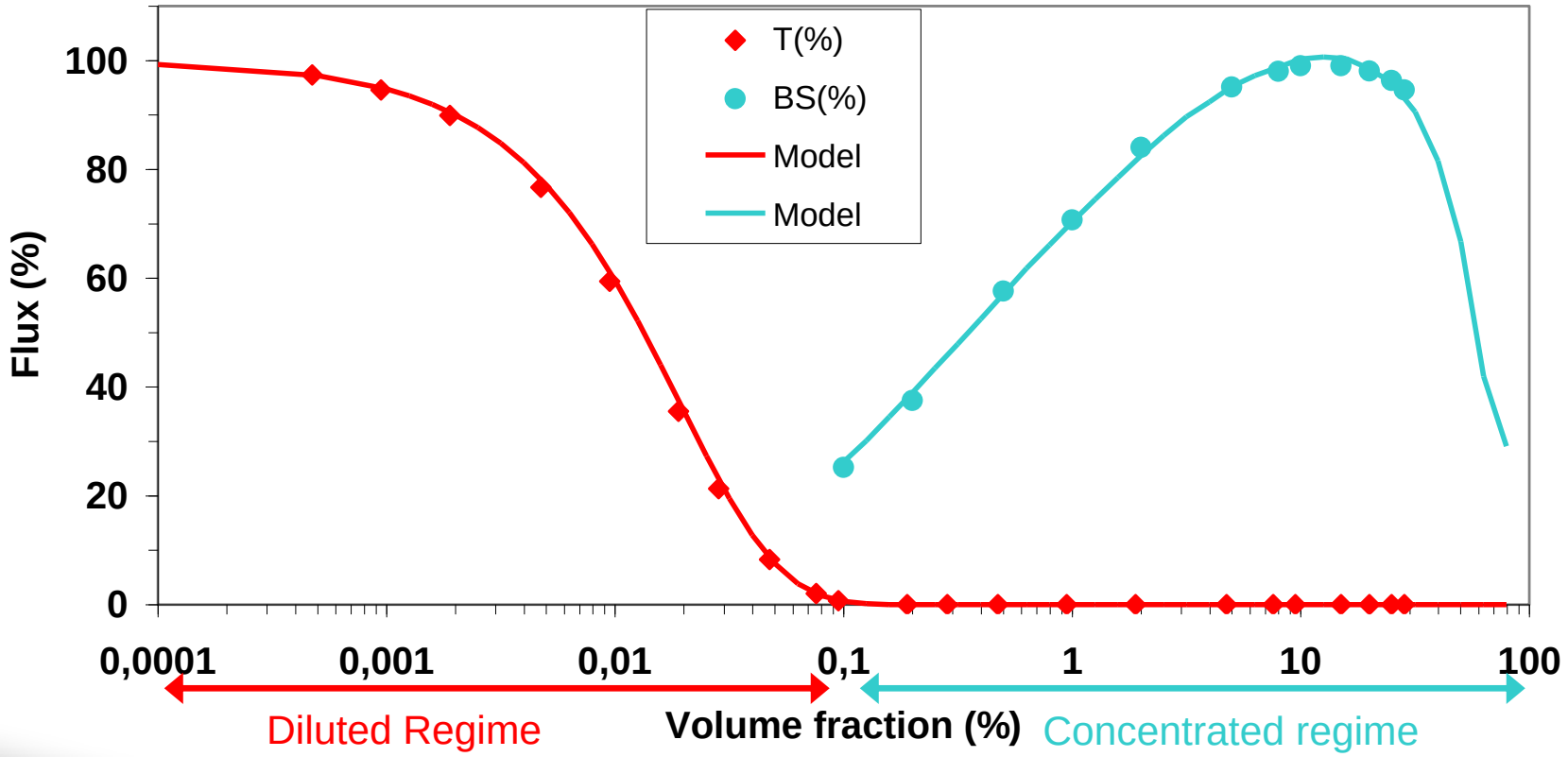
TURBISCAN TECHNOLOGY

How does it work?

Variation of particle concentration

ESTAPOR latex suspension (polystyrene in water)

d = 0.3µm, np = 1.59, nf = 1.33, Wavelenght = 880nm



Concentration range : from 0,001 to 95%

SMLS as a tool for size measurement

Why use the turbiscan for size measurements?

Measure concentrated samples

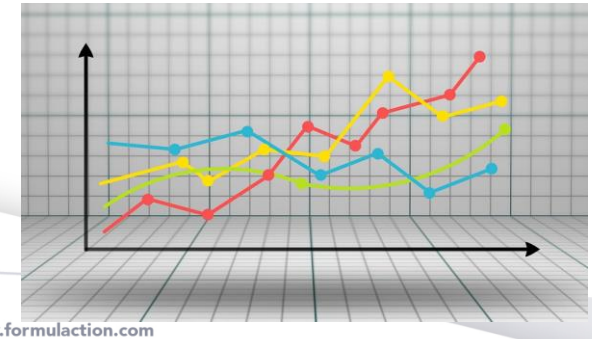
Non-Destructive

Simple – no lengthy preparation

1 Measurement in 25 seconds

Size measurements

Follow the evolution of the sample over time



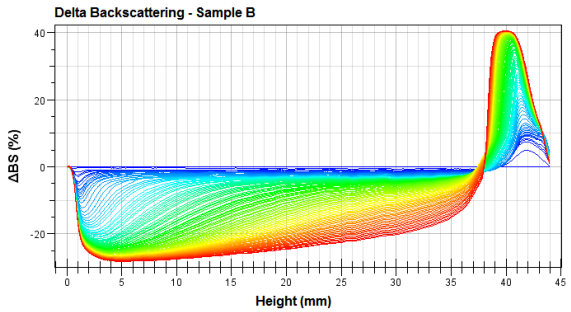
Average particle size measurements

Large particle size range

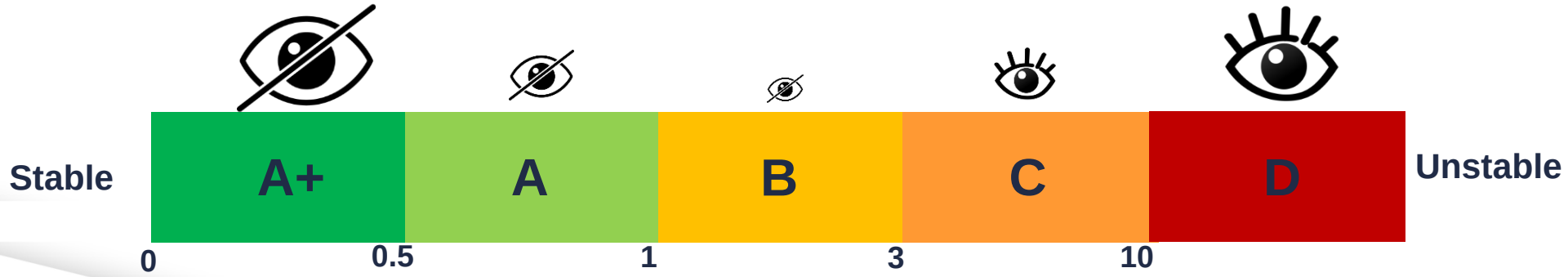
Turbiscan data
TSI

⇒ Ranking of stability thanks to TSI

Turbiscan Stability Index is THE stability parameter!



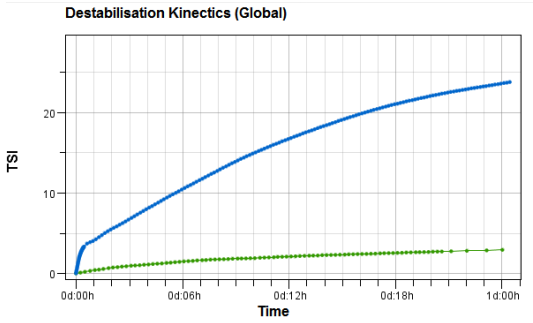
$$TSI = \frac{\sum_h |scan_i(h) - scan_{i-1}(h)|}{H}$$



Turbiscan data
TSI

tsi : the ultimate parameter for stability measurements

- One-Click parameter
- Easy, Pragmatic, Automatic and Fast Answer
- ONE unique number to rank & compare samples
- Takes in account ALL DESTABILIZATIONS
- The most suitable and robust tool to quantify and rank samples
- NO information required



⇒ The STABILITY CRITERIA

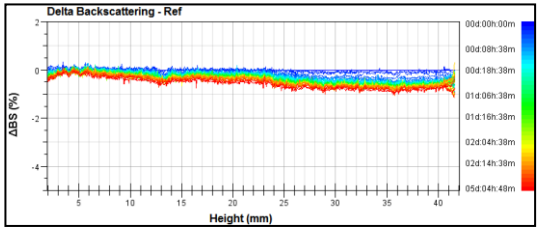
Applications

Turbiscan data
General application - optimization

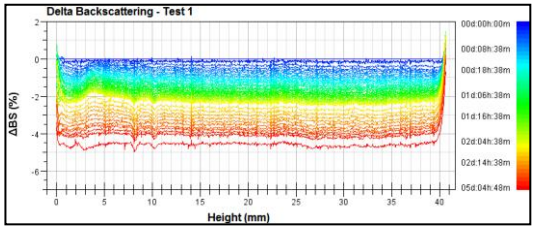
⇒ Step 1 : Identify the best surfactant

3 formulations :

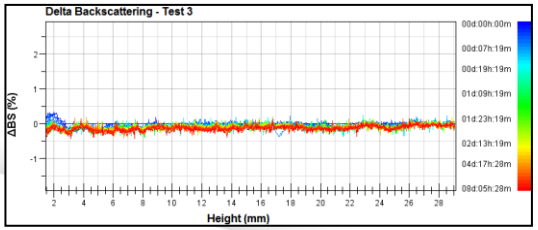
Reference

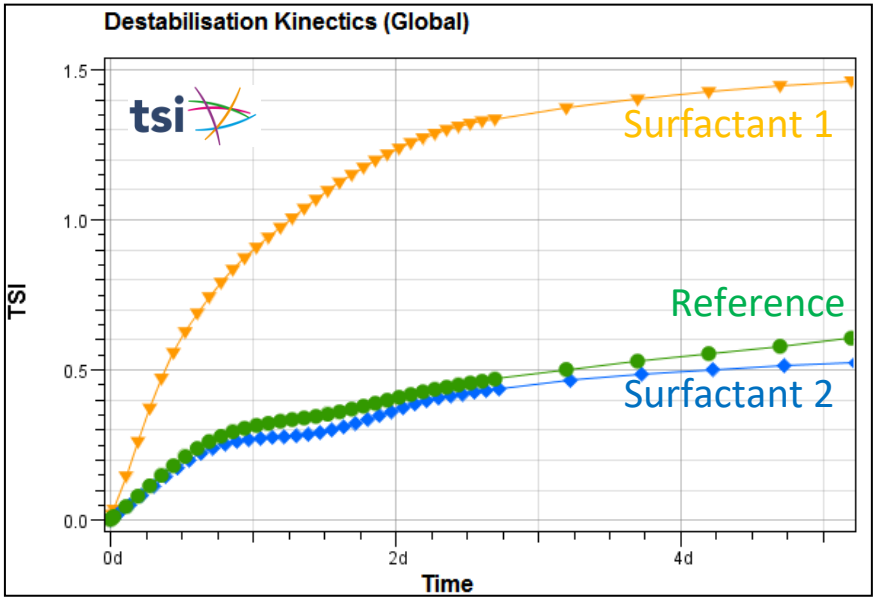


Surfactant 1



Surfactant 2



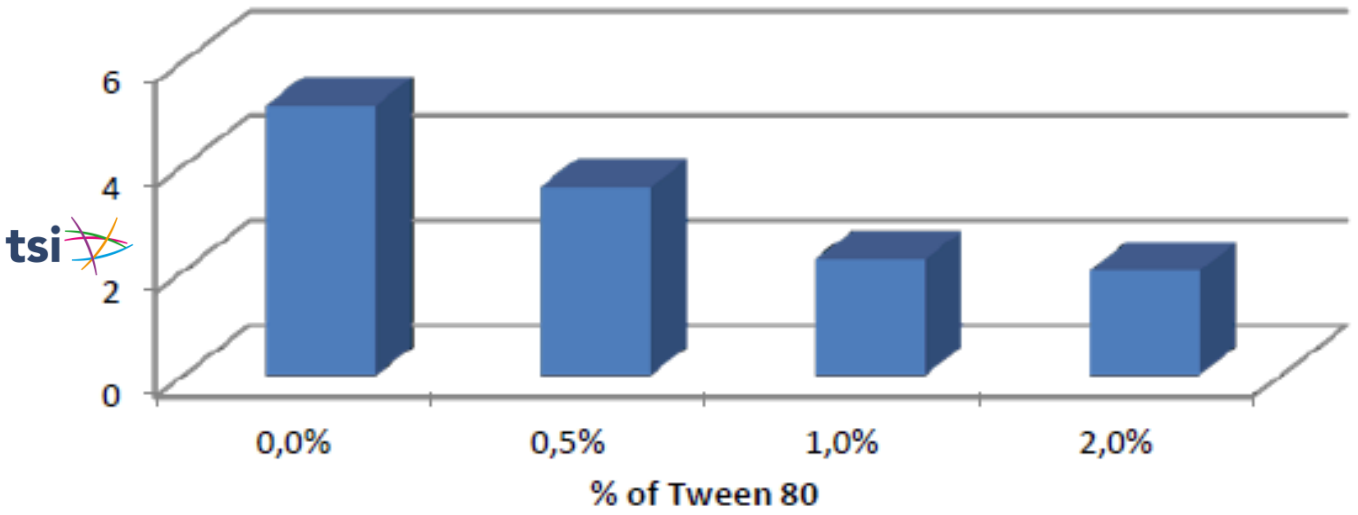


- ***Best Surfactant is the Surfactant 2***
- ***Answer in less <u>than 1 day</u>***
- ***Quantification with the TSI***

Turbiscan data
General application - optimization

⇒ Step 2 : How much surfactant should be used

Unstable



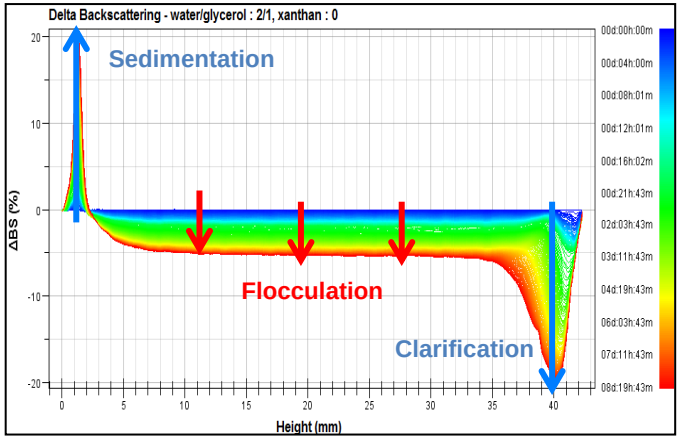
Stable

⇒ 1% of surfactant is the optimum concentration for this formulation

Turbiscan data
General application - stabilizers

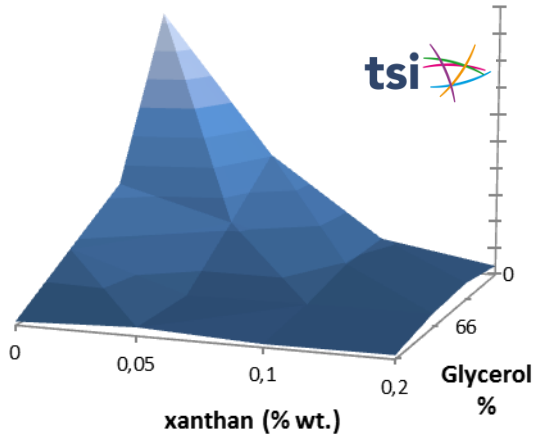
⇒ Stabilization by viscosity increase : Adjust the use of the polymer

- *Use of the experimental design + TSI*
- *16 formulations*



Particle size variation + Migration

Unstable



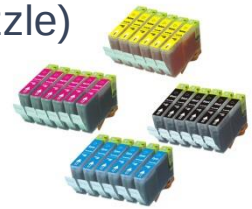
Stable

The amount of stabilizer can be optimized to adjust effectiveness and price

Turbiscan applications
Migration of pigment

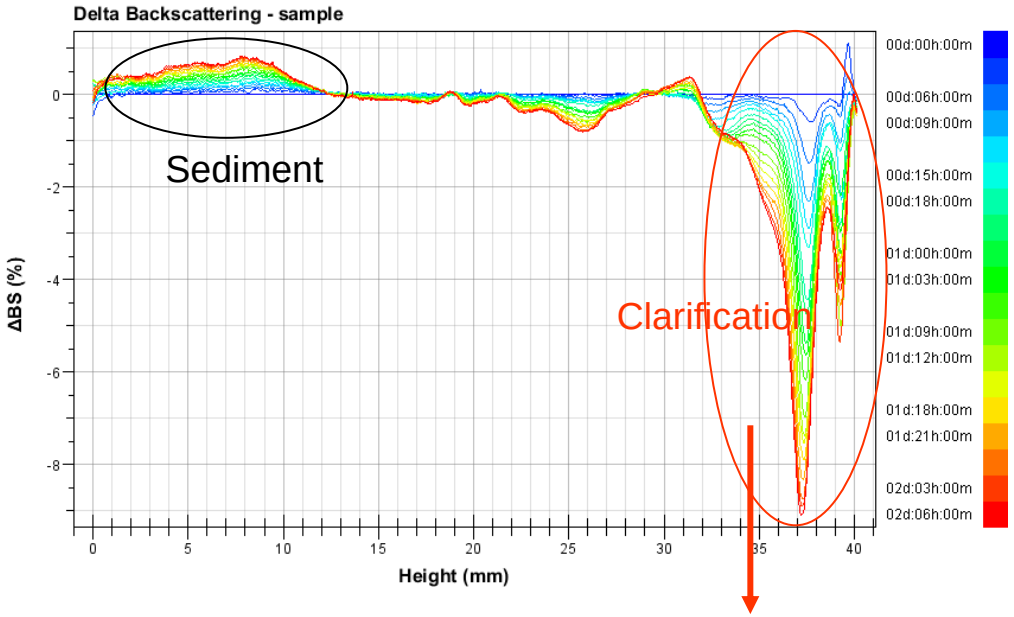
- **Problematic :** pigment tend to settle because of density difference

- **Solution** : - increase viscosity (limited to 3mPa.s with some inkjet nozzle)
  - decrease particle size (induce colour changes)



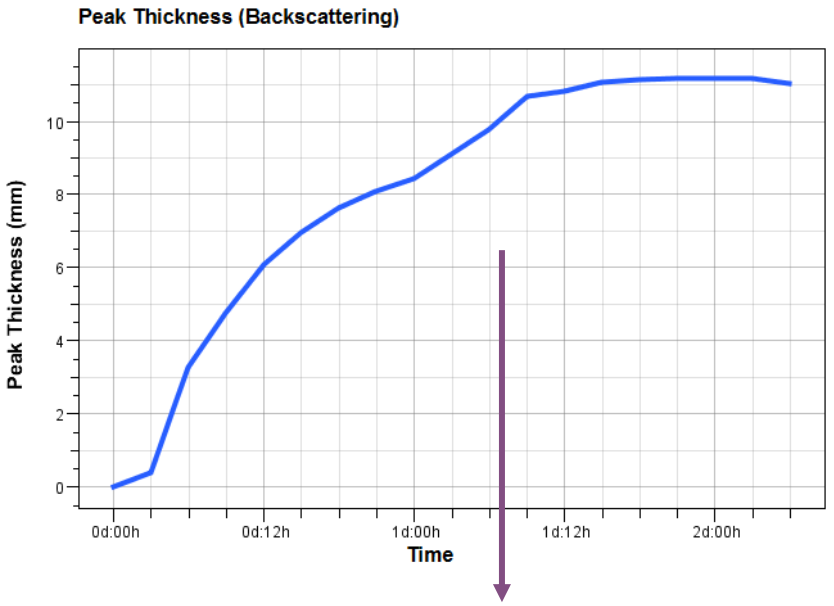
- **Objective**: find the best comprise and test the best formulation

Turbiscan applications
Migration of yellow pigments



2 peaks = 2 populations of particles

Sediment thickness kinetics



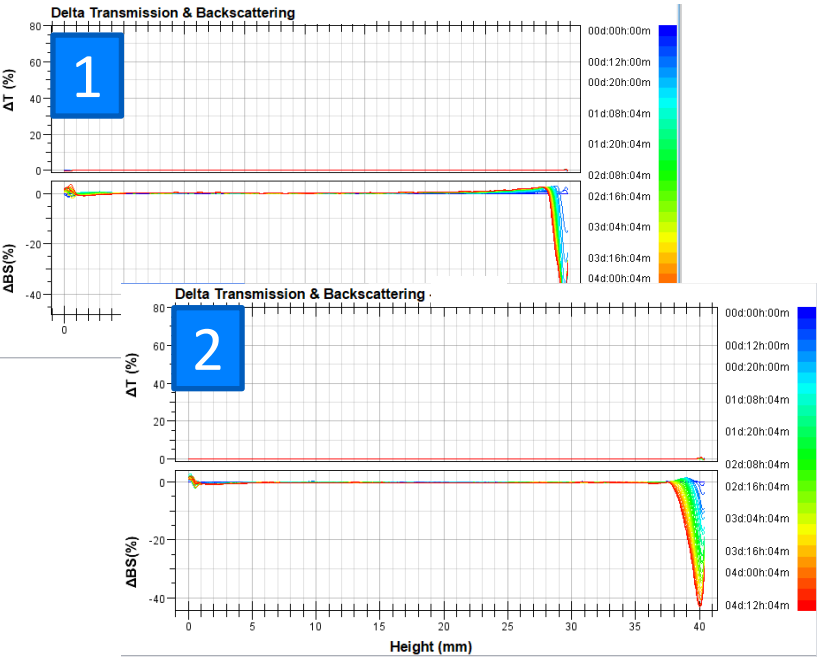
Migration velocity : 0.88 mm/d

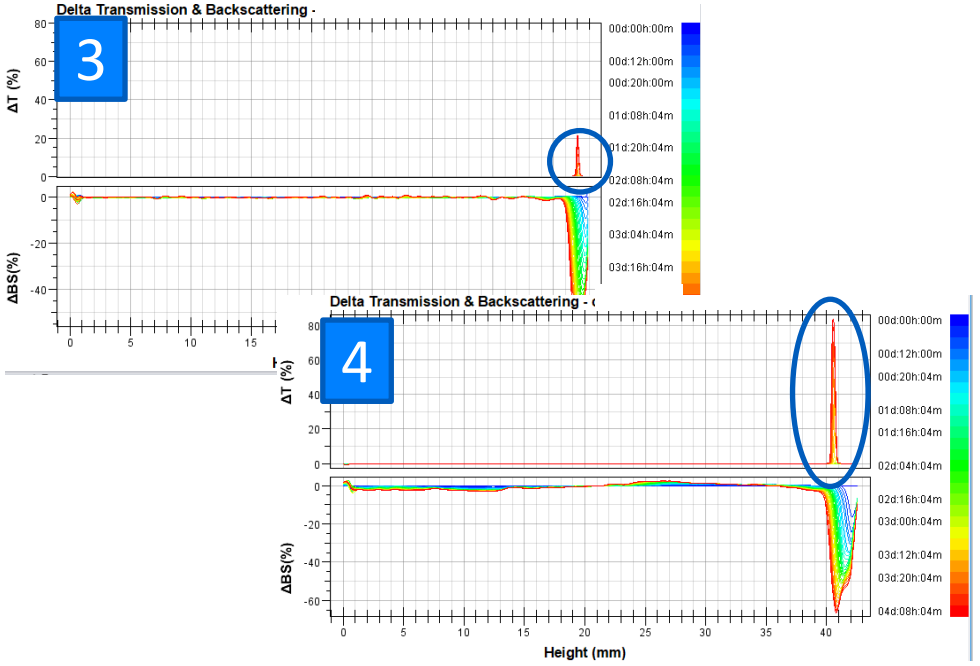
⇒ Detection only in the first hours

TSI Applications

Road Paint

- 4 different road paints were tested to determine their stability
- These samples are highly concentrated in pigment– no problem for the turbiscan
- 2 different solvents were used



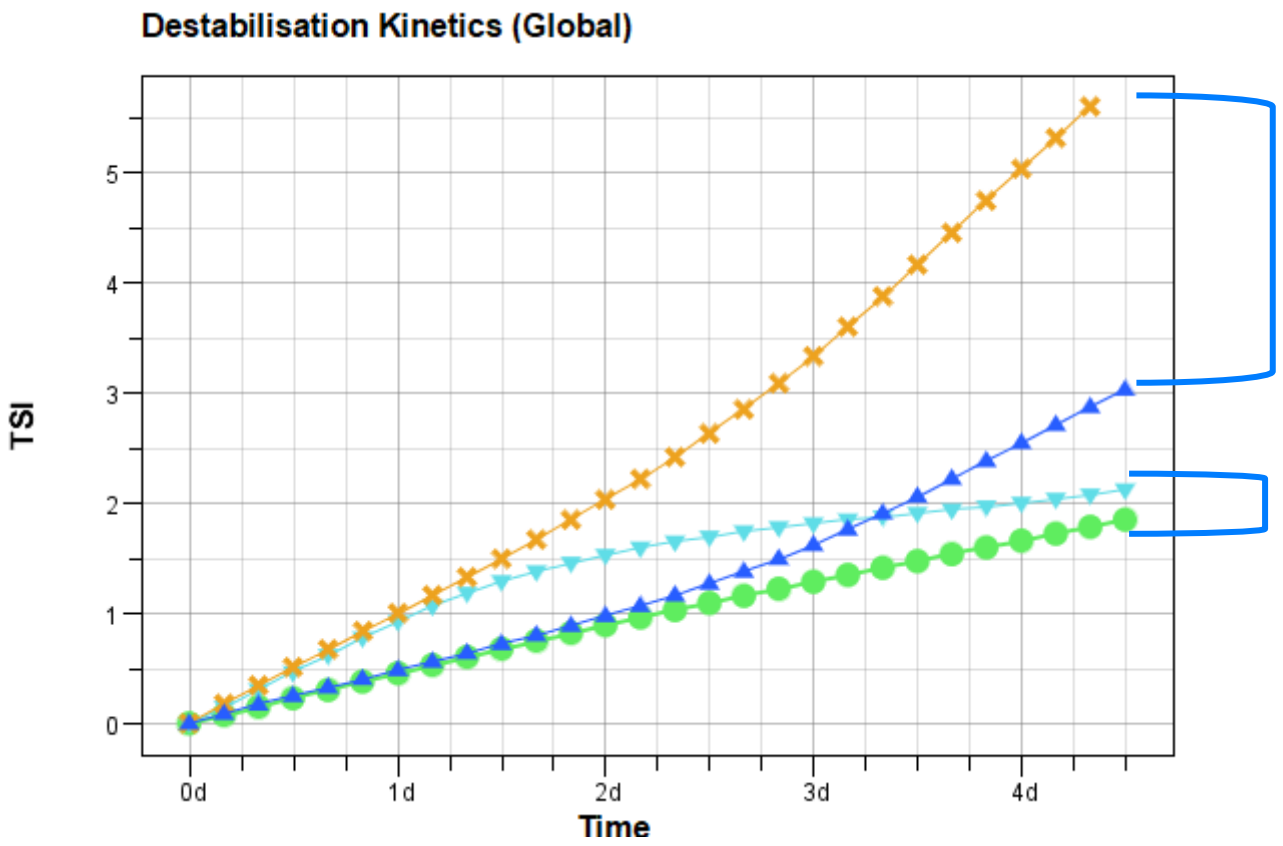


Solvent A

Solvent B

TSI Applications

Road Paint



✓ Solvent A gives paint that is more stable

✓ Results obtained in 4 days

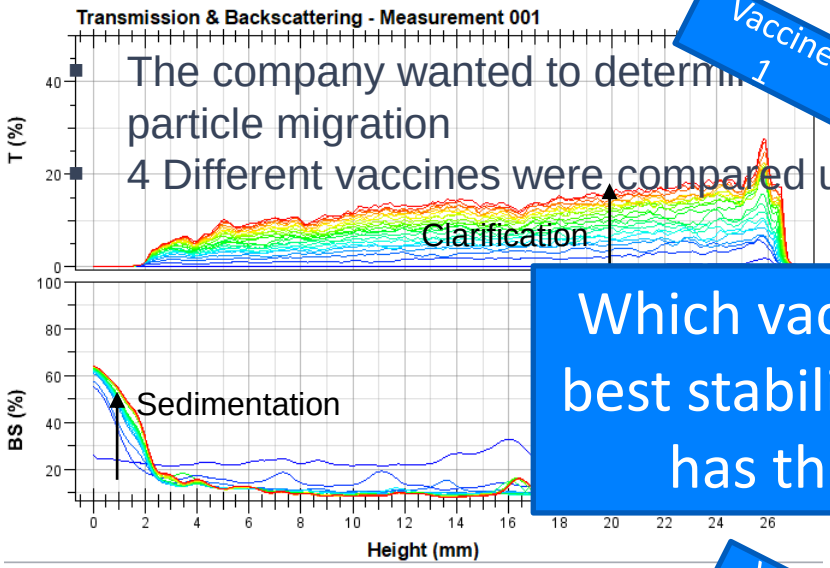
Turbiscan applications
PHARMACEUTICALS

TSI Applications
Sedimentation in Vaccines

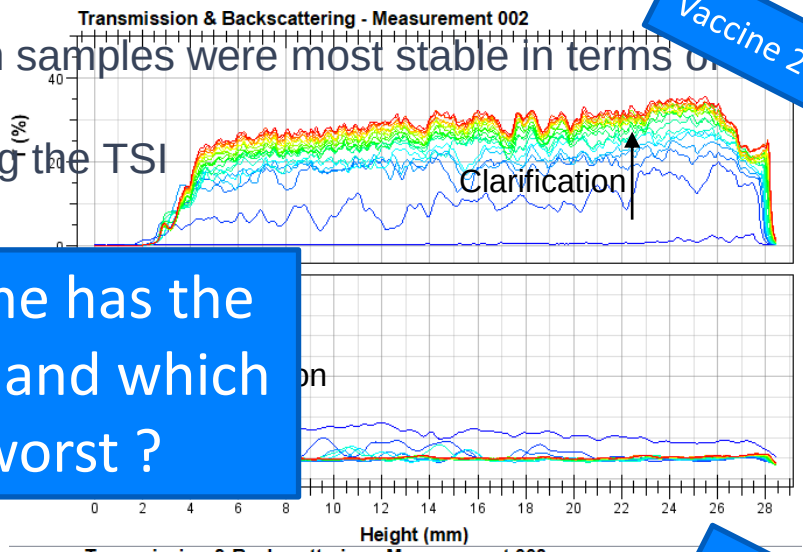
- The company wanted to determine which samples were most stable in terms of particle migration
- 4 Different vaccines were compared using the TSI

Which vaccine has the best stability and which has the worst ?

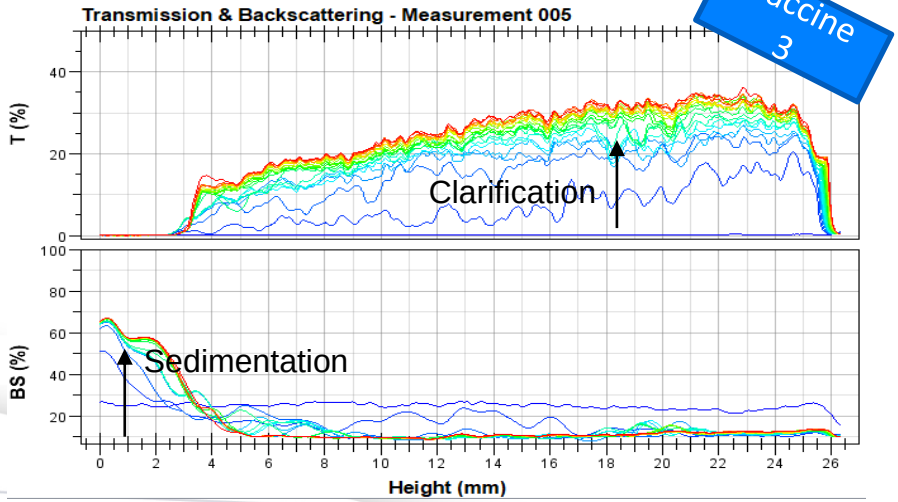
Vaccine 1



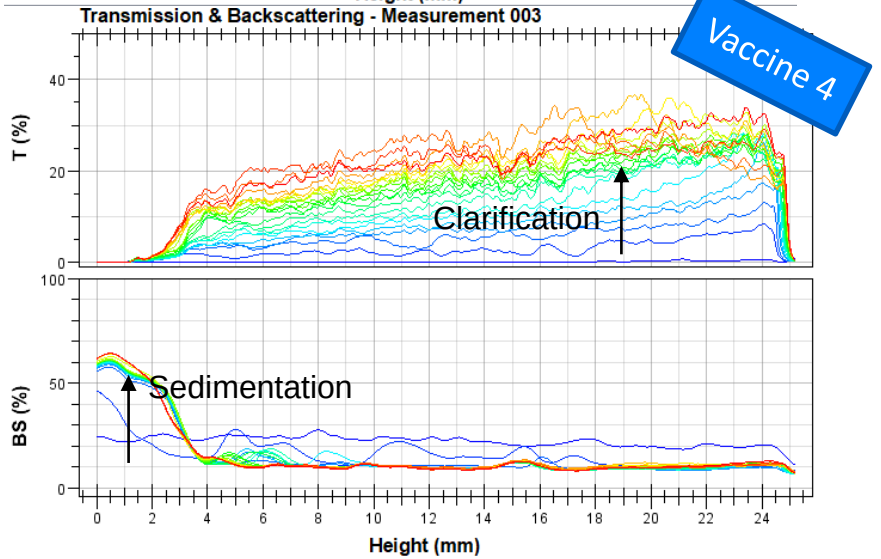
Vaccine 2



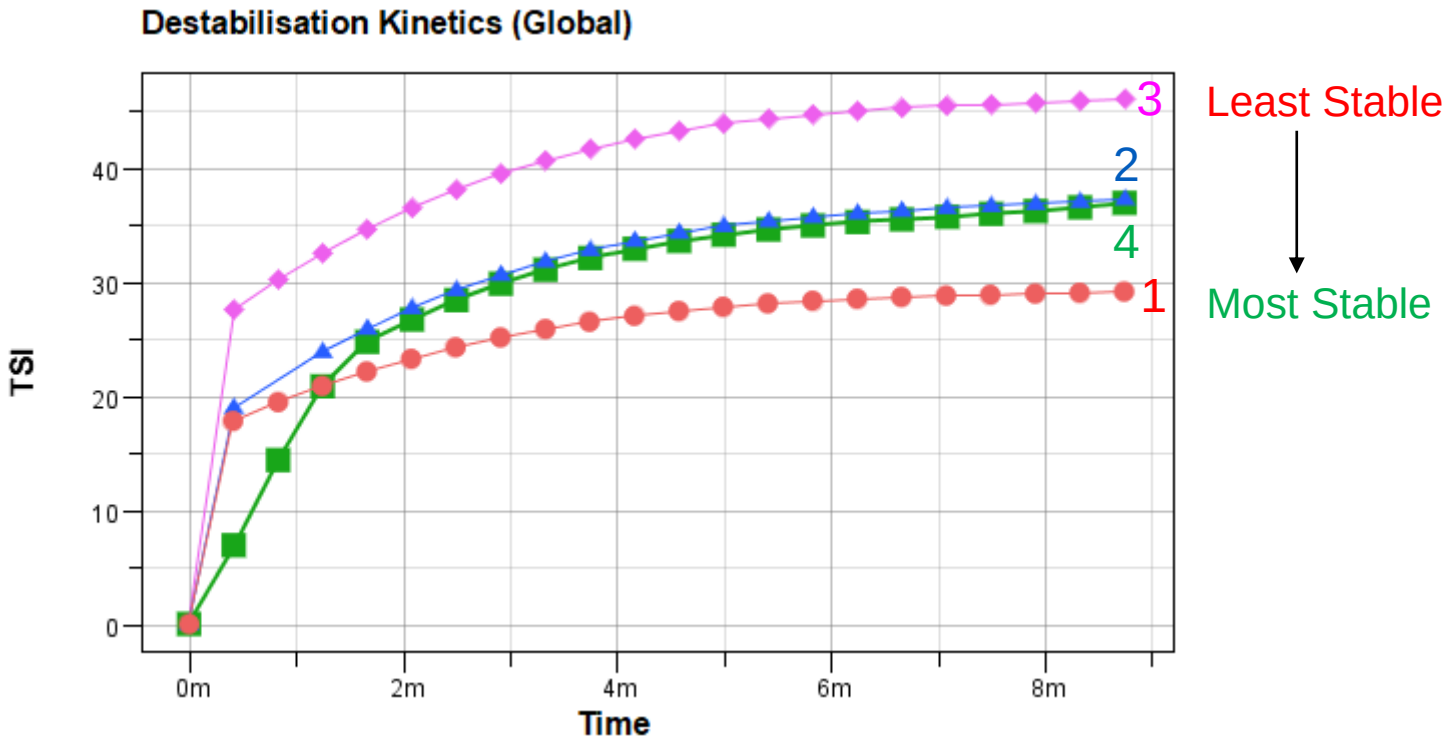
Vaccine 3



Vaccine 4



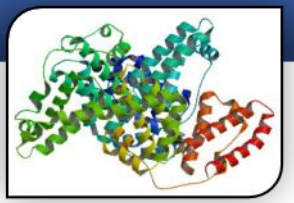
TSI Applications
Sedimentation in Vaccines



- After **8 minutes** of analysis they could see which samples had a better stability

Protein denaturation with temperature

BSA protein – Pharmaceutics field



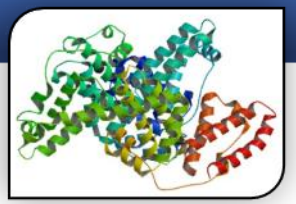
- **Problematic**: Temperature increase leads to proteins denaturation which consists in modifying interactions and going from transparent to opaque samples linked to size increase

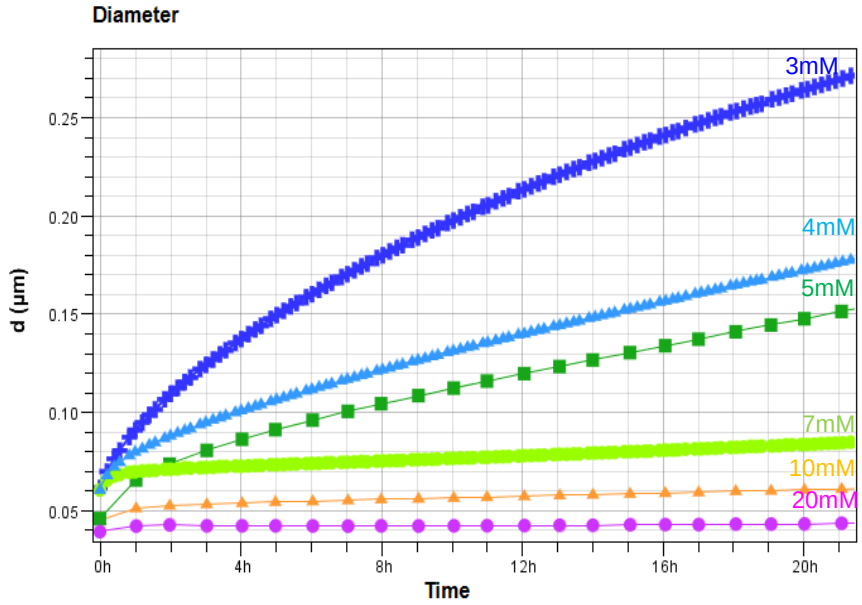
- **Solution**: Histidine, an amino-acid, is currently used to protect therapeutical protein against denaturation.

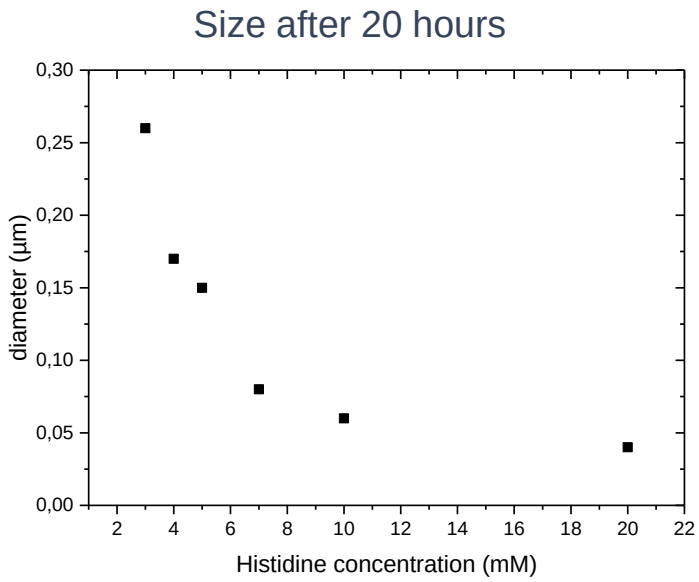
- **System**: 8 samples of BSA 10%wt with different amount of histidine (mM) were analysed at 60° C

Protein denaturation with temperature

BSA protein – Pharmaceutics field







⇒ Increasing histidine concentration enables to keep lower diameter and closer to native state without denaturation

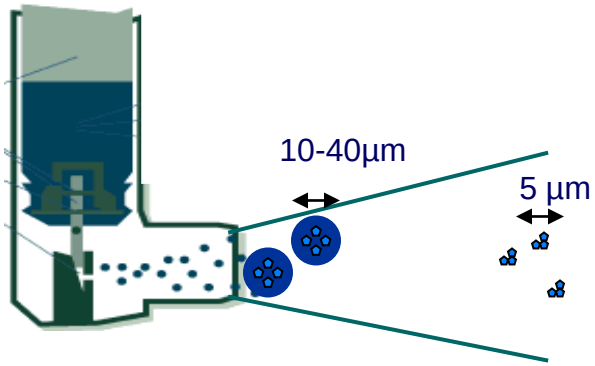
Turbiscan applications
Inhaler

- **Context** : Treatment of Asthma

Creaming

Or

Sedimentation



Evaporation of the propellant

↓

Drug particles into lungs

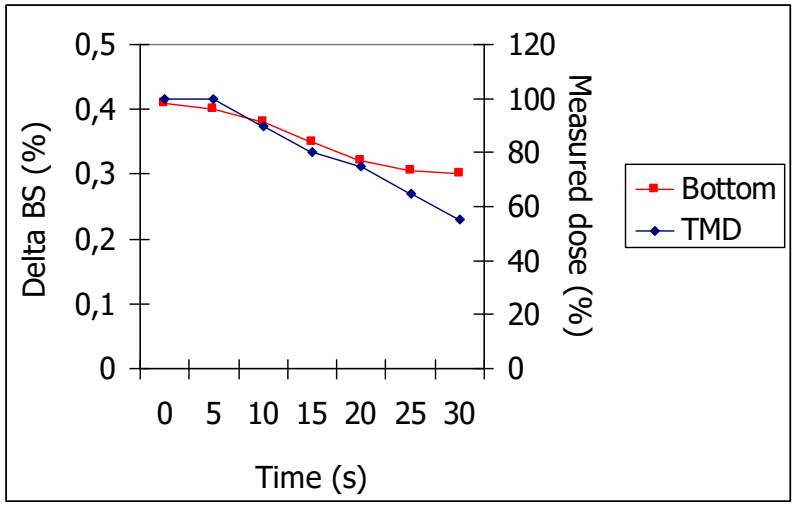
- **Requirements** :

- High and constant quality
- Same dose each time (25-150µL)
- Same amount of active per zone

Turbiscan applications
Inhaler

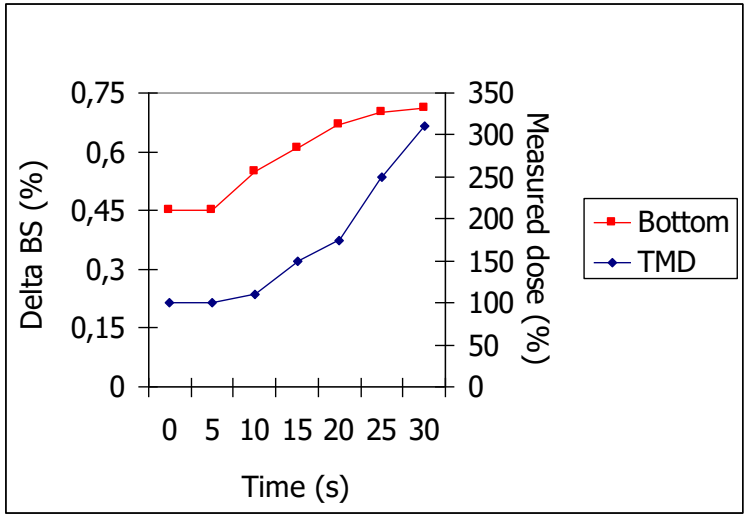
- **Correlation with timed medication delivery**

Creaming (bottom)



⇒ Insufficient dose after 10 s

Sedimentation (Top)



⇒ Too much dose after 10 s

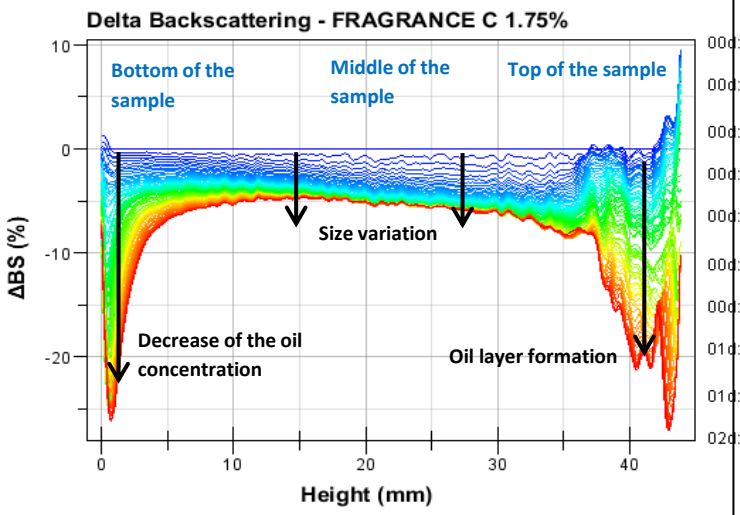
Turbiscan applications
HOME & PERSONAL CARE

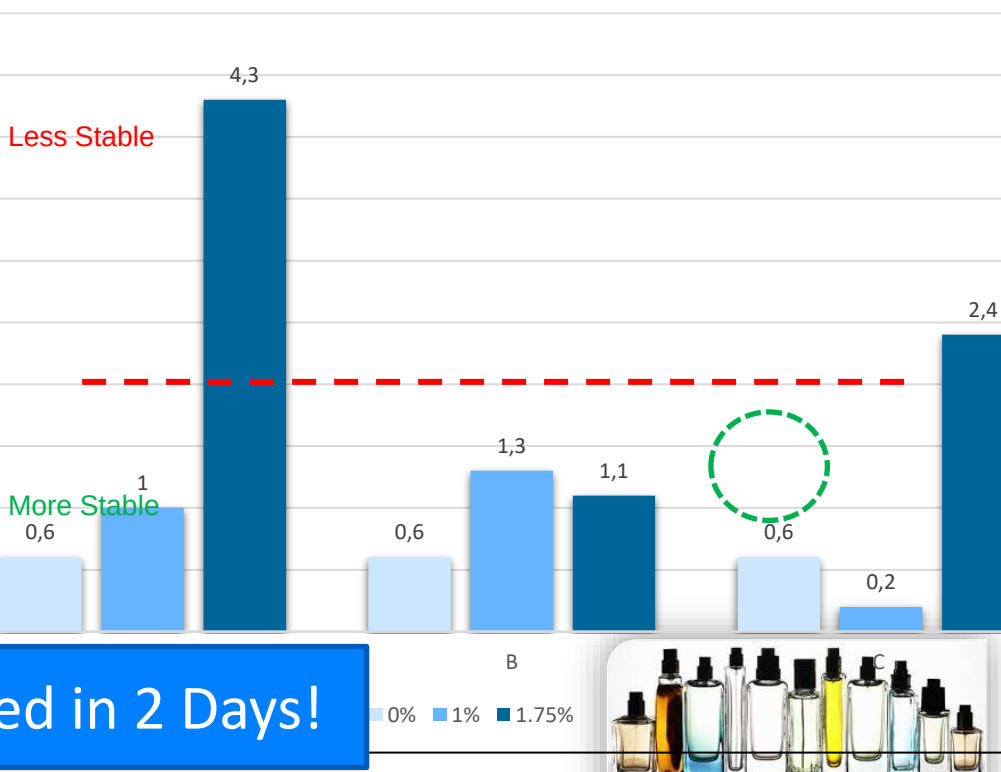
TSI Applications

Perfume stability with different fragrances

Givaudan

- Aim – Determine the stability of emulsions with added fragrances
- Fragrance A, B and C tested in the ~~same emulsions, concentrations: 0%, 1% and 1.75%~~
- Usual test – 45 days at 45ºC





Results Obtained in 2 Days!

Turbiscan

TSI Applications – Perfume stability with different fragrances

- Aim – Determine the stability of emulsions with added fragrances
- Fragrance A, B and C tested in the same emulsions, concentrations: 0%, 1% and 1.75%
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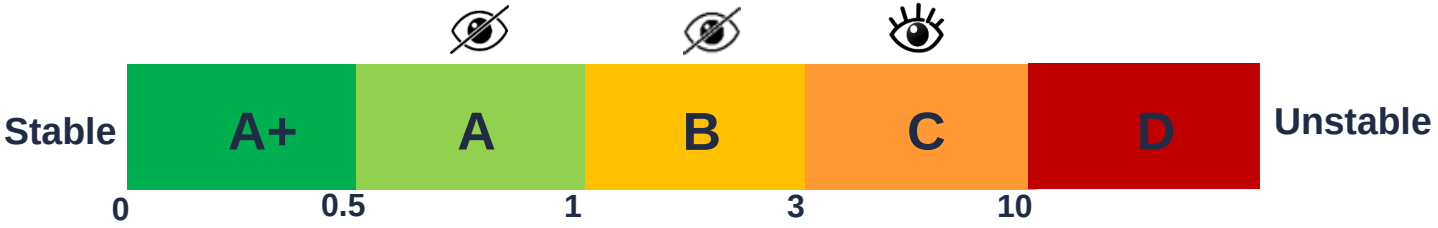
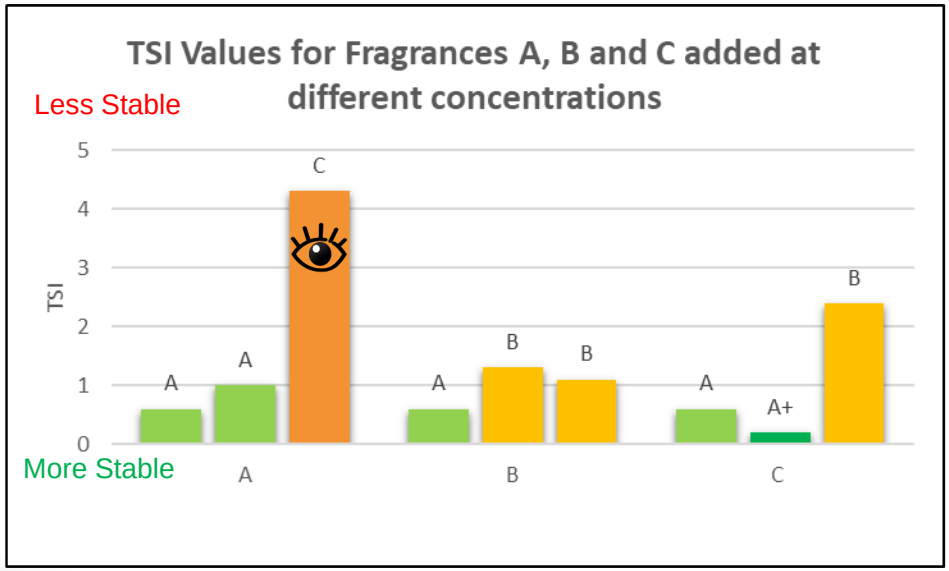
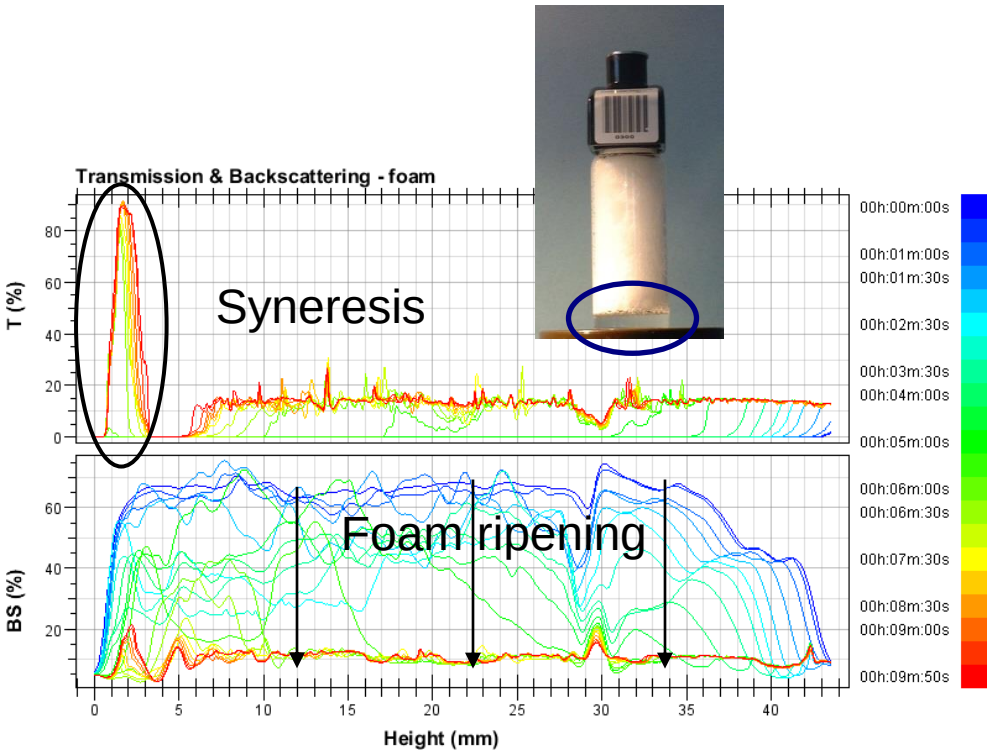
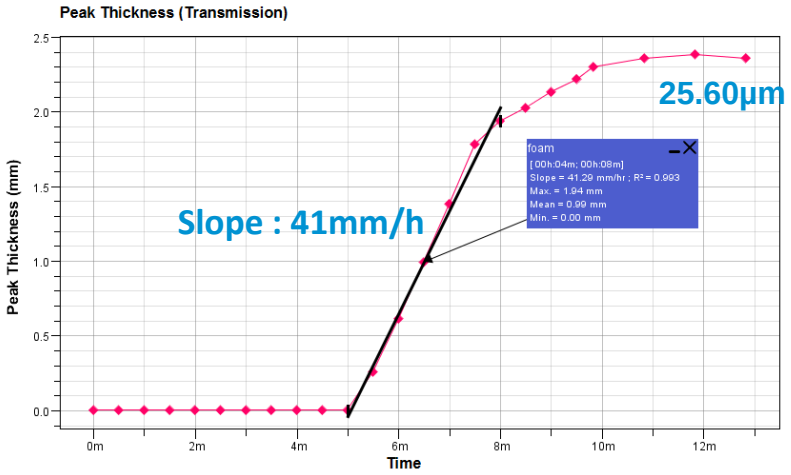




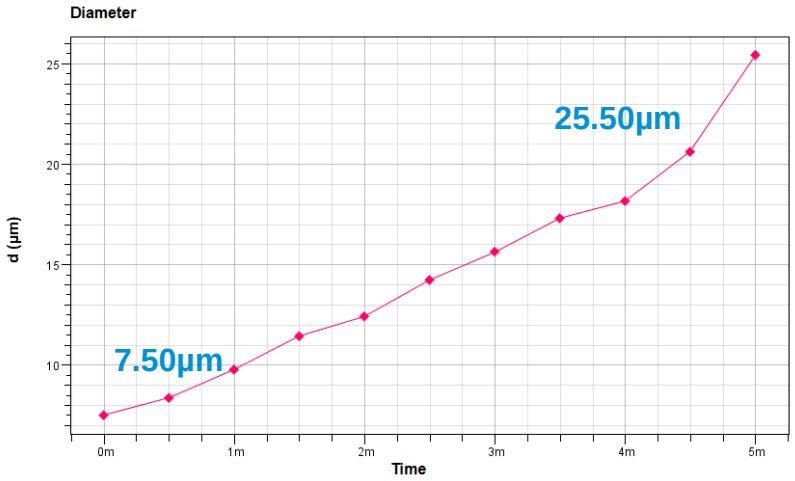
Turbiscan applications
Foam stability



- Drainage – Thickness of drainage phase



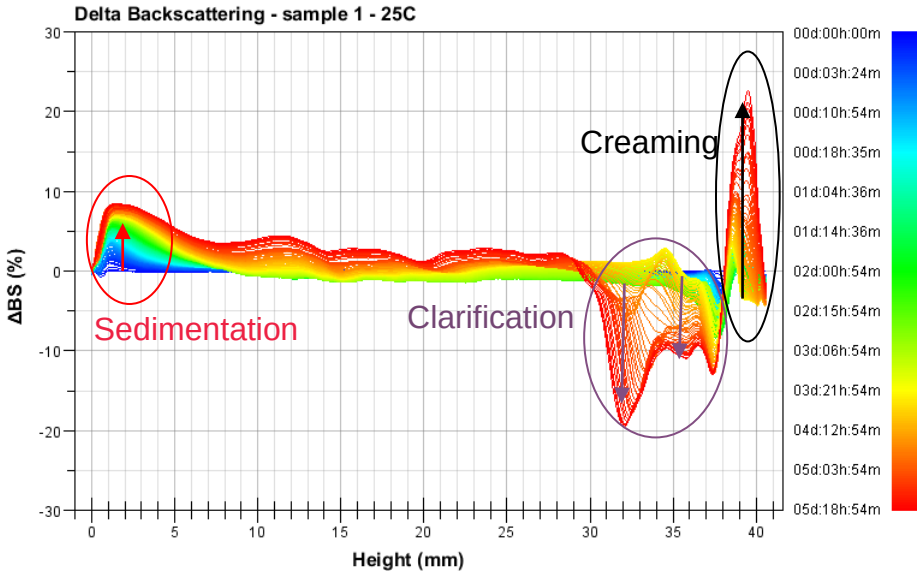
- Ripening – Diameter of bubbles



Turbiscan applications
FOOD

Turbiscan applications
Chocolate milk

⇒ Choise of optimal stabilizer for chocolate milk



- **Sedimentation :** compute migration velocity
- **Clarification**: follow phase thickness of clarification layer
- **Creaming** : follow phase thickness of cream layer

⇒ Different parameters for different phenomena

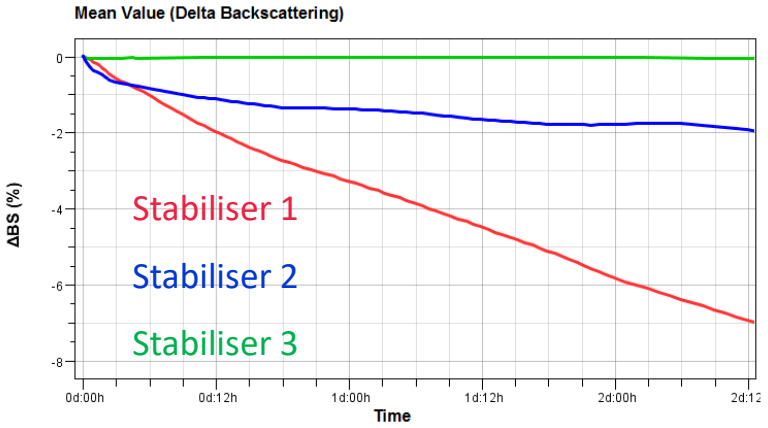
Turbiscan applications
Chocolate milk

⇒ Choise of optimal stabilizer for chocolate milk

From Sedimentation data

Stabilizer	Migration velocity (mm/h)
1	0.01
2	0.005
3	0.002

From Clarification data

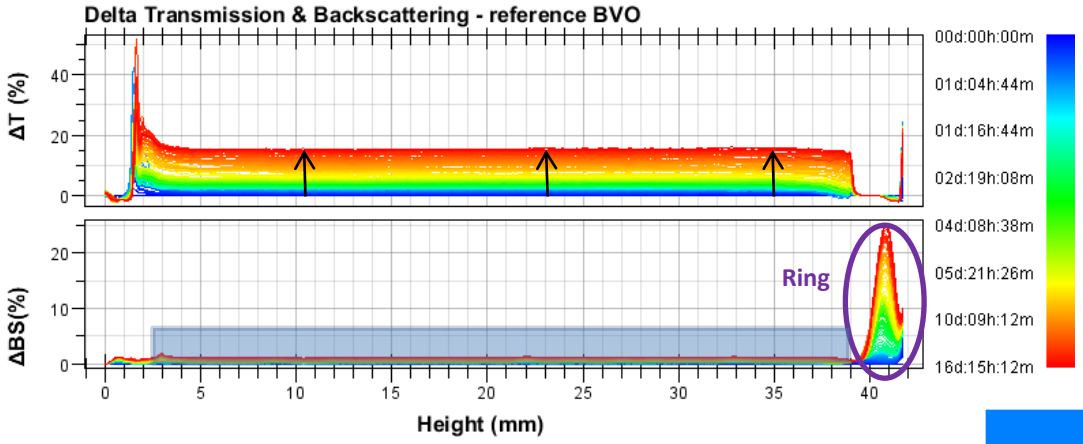


From global data

⇒ Stabilizer 3 is the most efficient

Turbiscan applications

Ring formation of beverages emulsions

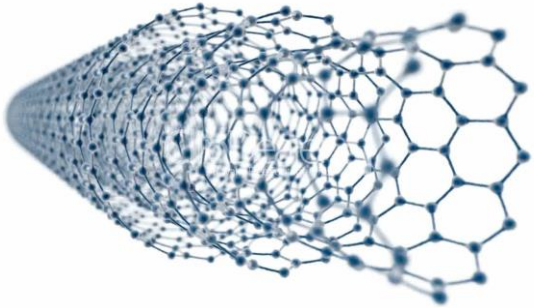


Sample	Delay before creaming (ring) (day)	Creaming rate(mm/day)	Final layer ring size (mm)
Reference BVO Weighting agent	2	0.58	1.6
New Weighting Agent	4	0.36	1.5

⇒ Ring (creaming layer) detected

⇒ New Weighting agent more efficient than the reference

Turbiscan applications
ELECTRONIC



Turbiscan applications
Carbon nanotubes

- **Context** : Carbon NanoTubes (CNT) are used to bring specific technical properties to materials (mechanical, electrical, thermal…)

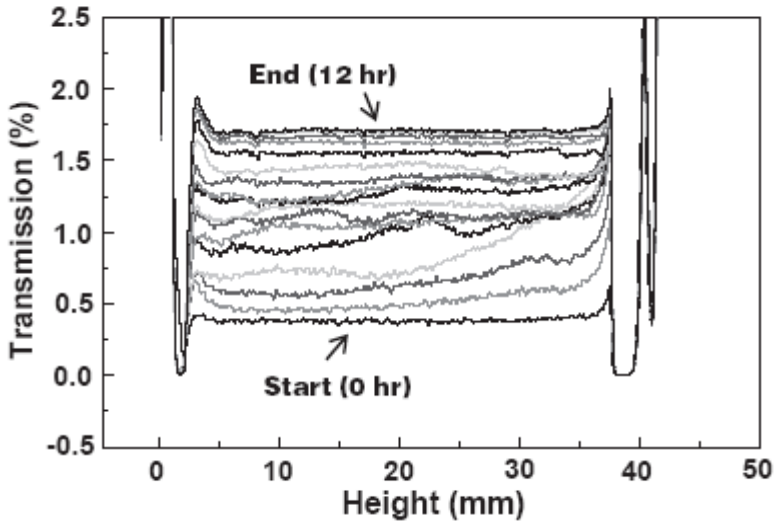
- **Properties :**

- Extreme Van der Waals interactions
- High aspect ratio

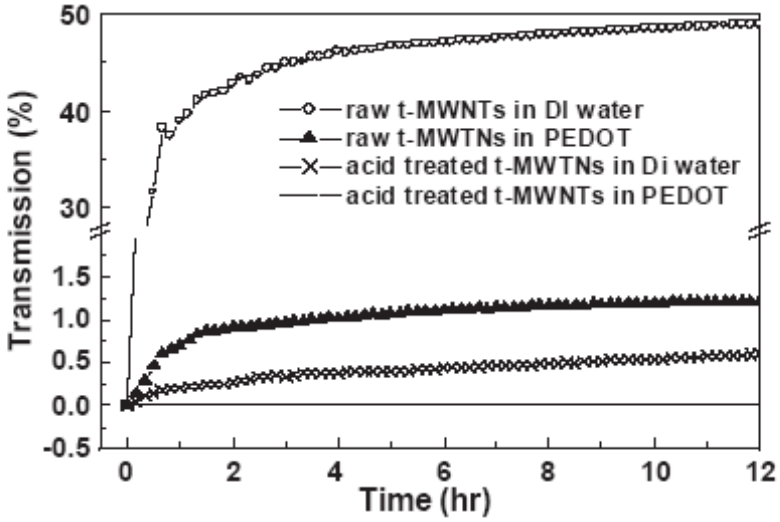
- **Problematic :** need to assess to dispersibility of CNT

Turbiscan applications
Carbon nanotubes

- **RAW t-MWNT In PEDOT**



- **Effect of solvent and acid treatment on stability**



⇒ Surface modification of CNT enables to improve dispersibility

J.B. Yoo, et al., Diamond and related materials, 14 (2005) 1882-1887

TURBISCAN Technology
Product Range

Basics	The Reference	6 times better 4-80°C	High throughput analysis
1	1	6	54
No	RT-60°C	4-80°C	RT-60°C
	tsi	tsi	tsi
			
Turbiscan Classic	Turbiscan Lab	Turbiscan Tower	Turbiscan AGS

TURBISCAN
Formulation World

World of Formulation

Dispersibility
Make sure the suspending matrix and process are well adapted to minimized the energy

Size
Particle size in the native media and if any variations with time

Redispersion
If destabilization, Is it reversible ?
Energy required ?

Stability
…llowed over time is
…or within the level
of acceptation. Shelf life

pascal.dacosta@formulaction.com

Sample testing and demo : contact Golik

More Application notes on www.formulaction.com

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