Technische Universität Braunschweig

pvz Zentrum für Pharmaverfahrenstechnik

New trends of individualised medicine at the Center of Pharmaceutical Engineering

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Background of Center of Pharmaceutical Engineering

Chemical synthesis

Extraction from plants

Microbiological production

Formulation

ABDA

Active pharmaceutical ingredient

Solubility

Sensitivity

Medicine

Meet the individual patients requirements

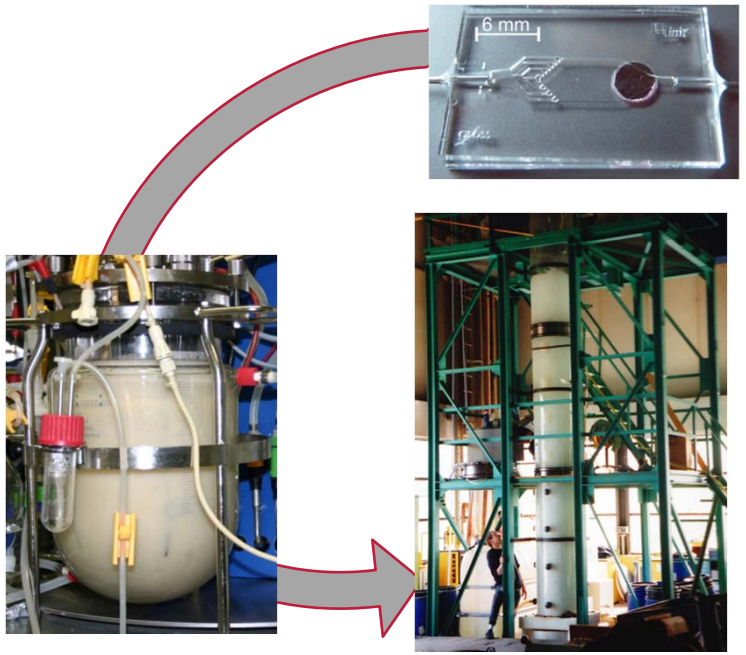
Costs

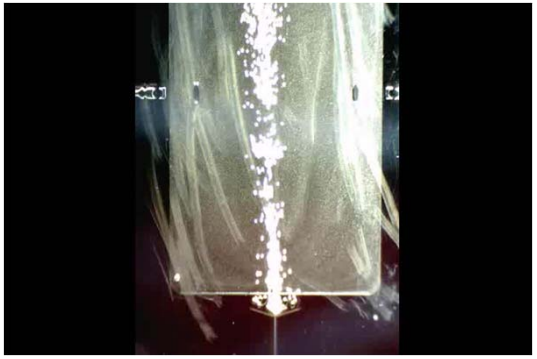
How can efficient and more and more individualised medicine be designed and produced with low costs?

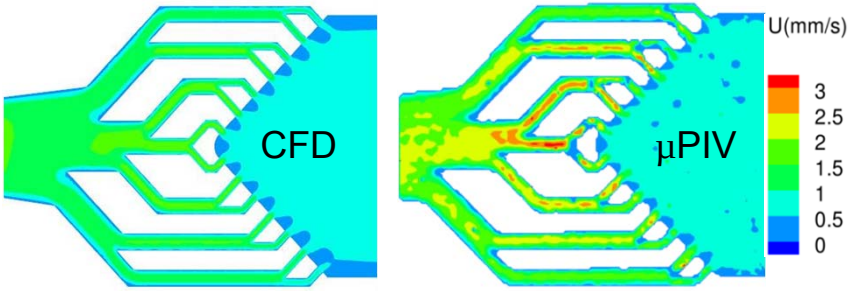
Center of Pharmaceutical Process Engineering
Main objectives

Low costs of medicine

- Development of customized and cost-effective processes at **different scales**
- Development of **design methods** based on very small amounts of product
- **Continuous production** of API and medicine (solid and liquid forms)





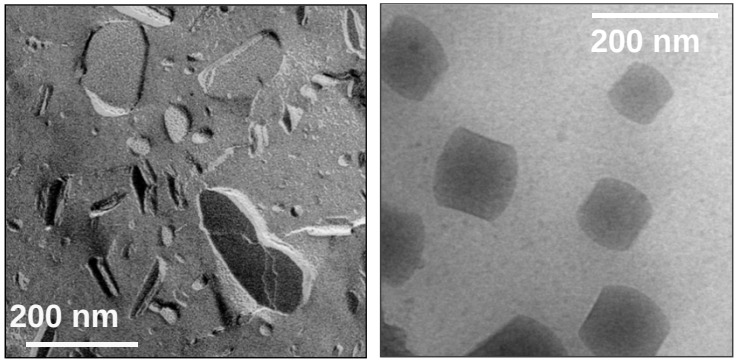


IMT, ibvt

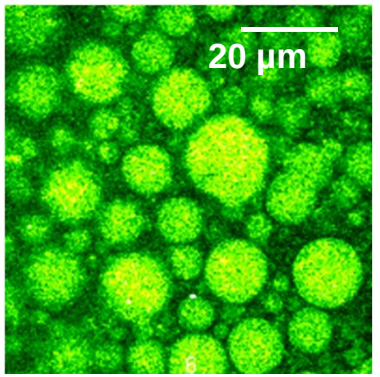
Center of Pharmaceutical Process Engineering
Main objectives

Efficient medicine

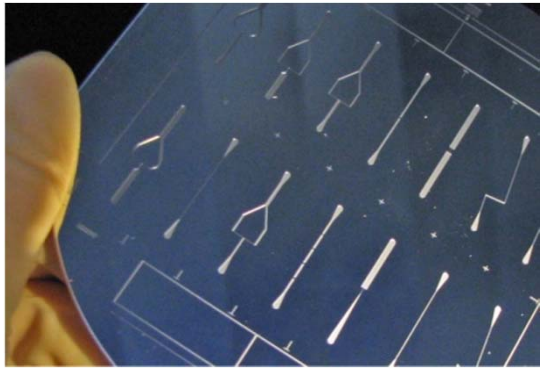
- **Increased bioavailability** by new formulations and new ways of processing for poorly water soluble drugs
- **Careful processing** of sensitive (macromolecular) drugs
- Methods for **development with small quantities**



IPhT



IPhT, IPC

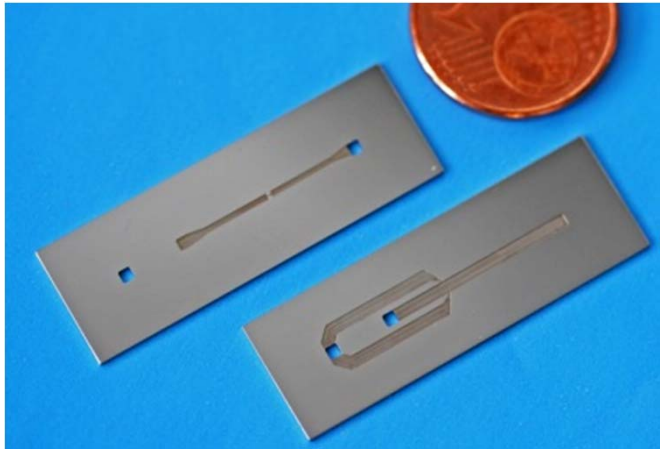


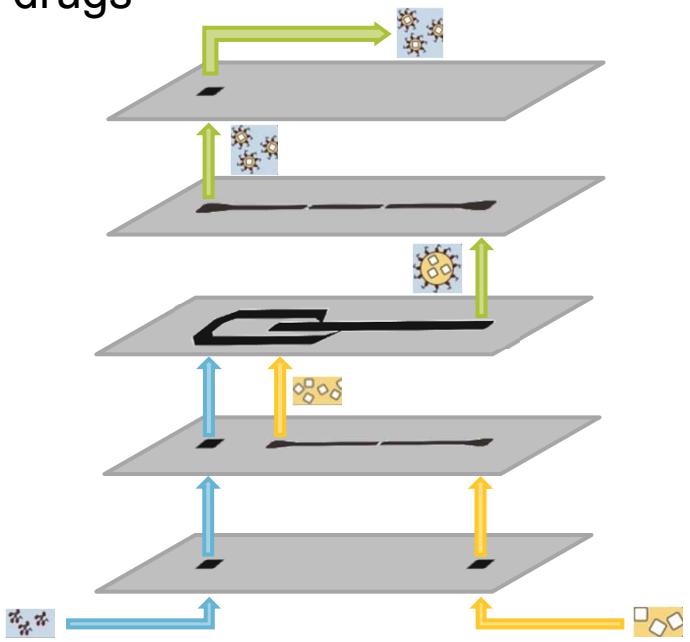
IMT

Center of Pharmaceutical Process Engineering
Main objectives

Personal/Individualised medicine

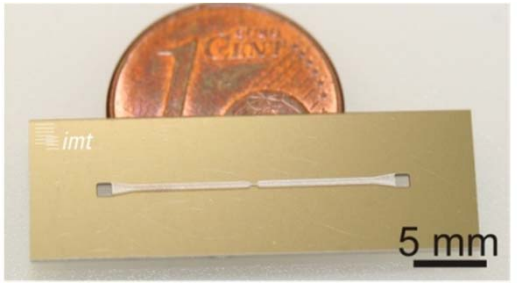
- Processing or **manufacturing of individual drugs and medicines** tailored to each patient
- Development of **miniaturized factories** for drugs and active substances



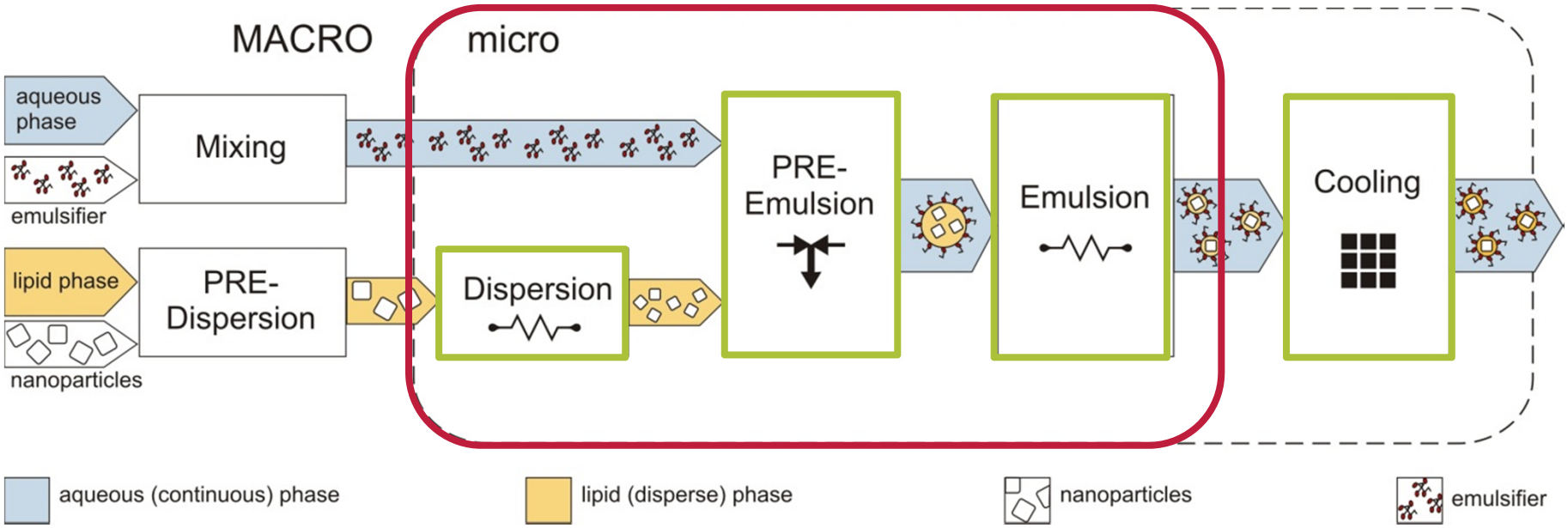


Research Example: Development of modular overall microsystem within German research program „mikroPART“

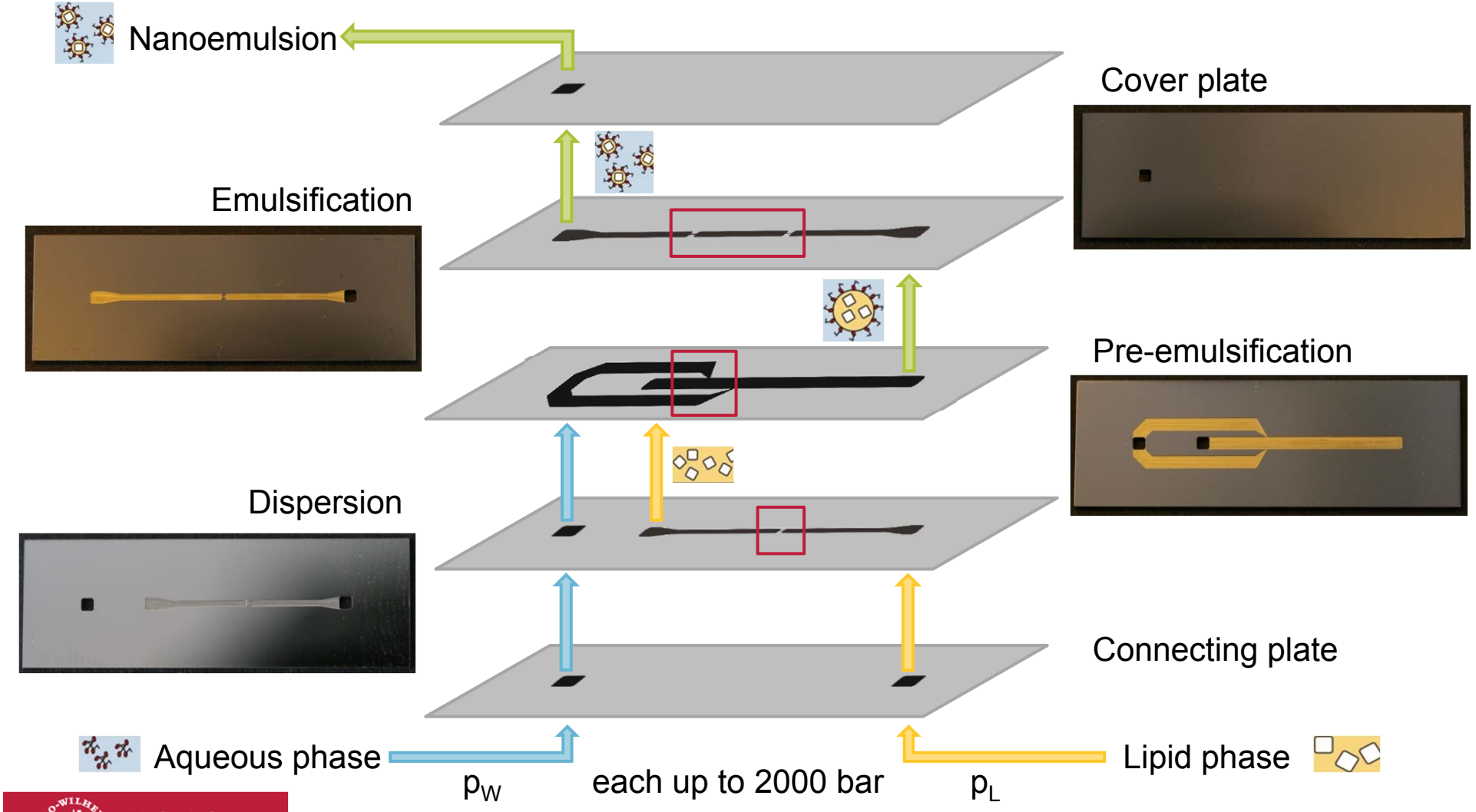
- Continuous dispersion production
- Separate dosing of aqueous (continuous) and lipid phase
- Very small equipment volume and, thus, high potential for production of small quantities of individualized product



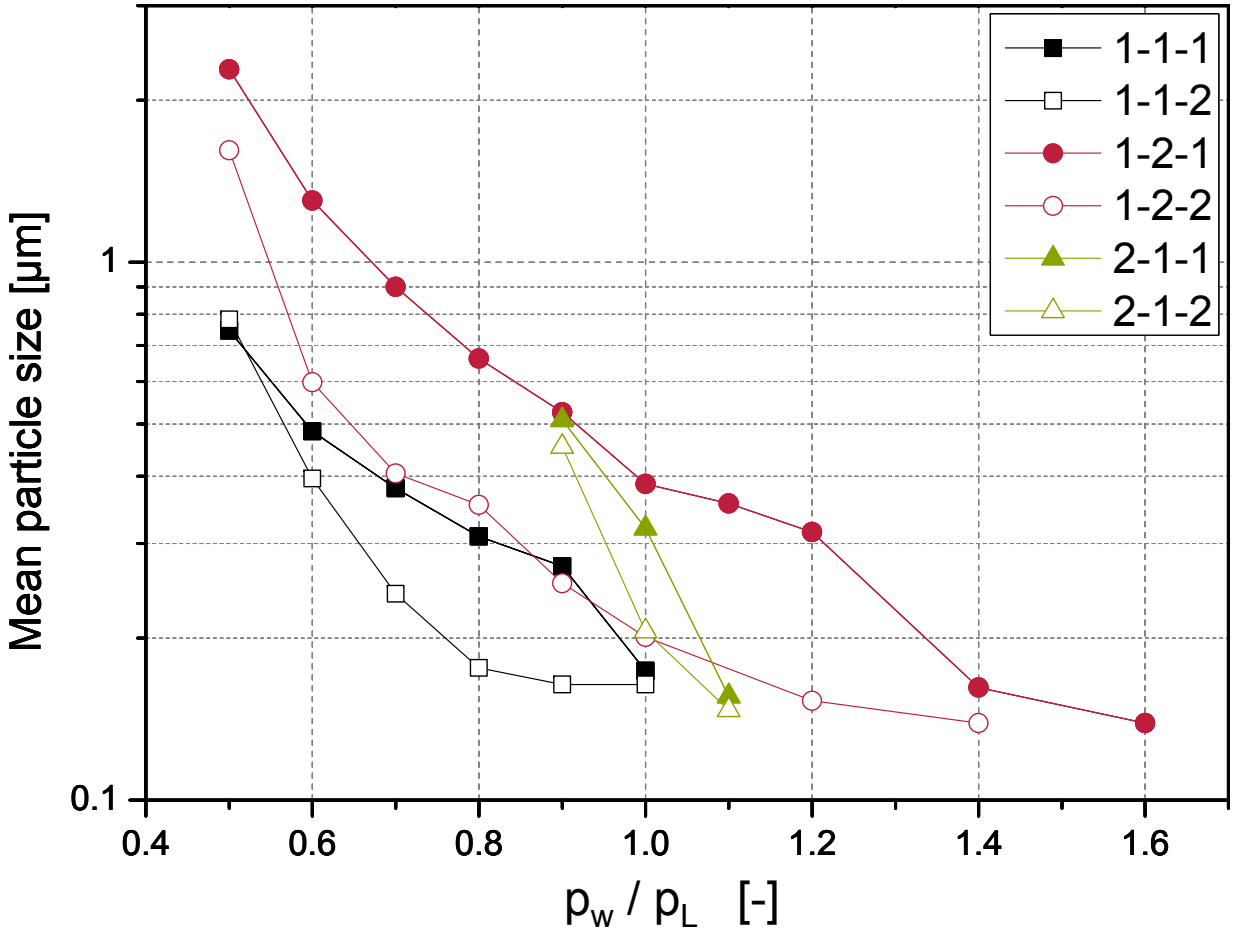
mikroPART

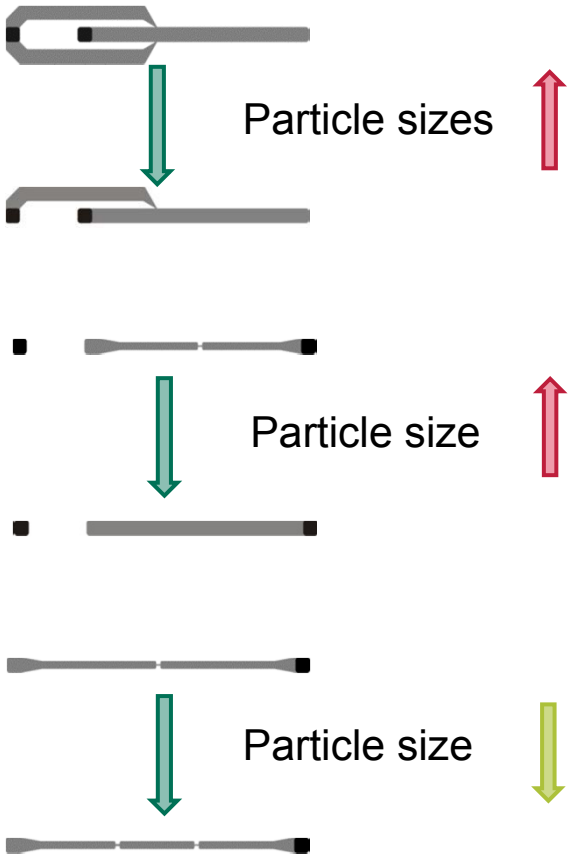


Modular assembly of the overall microsystem



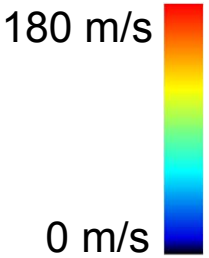
Influences on the particle size



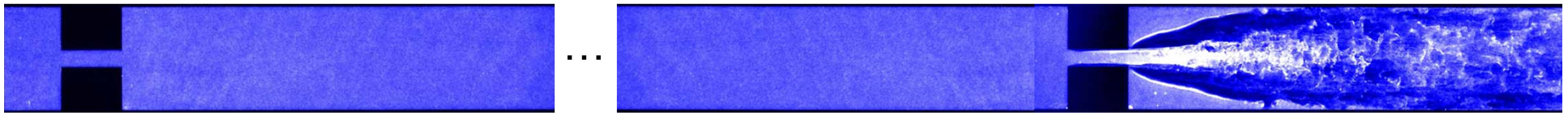


p_L = 1000 bar

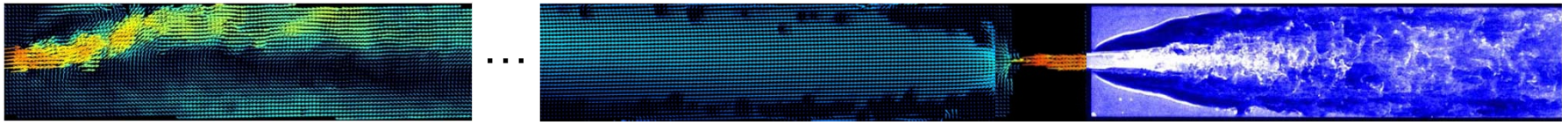
Fluid flow in the double orifice channel



Δp = 200 bar p_C = 0 bar

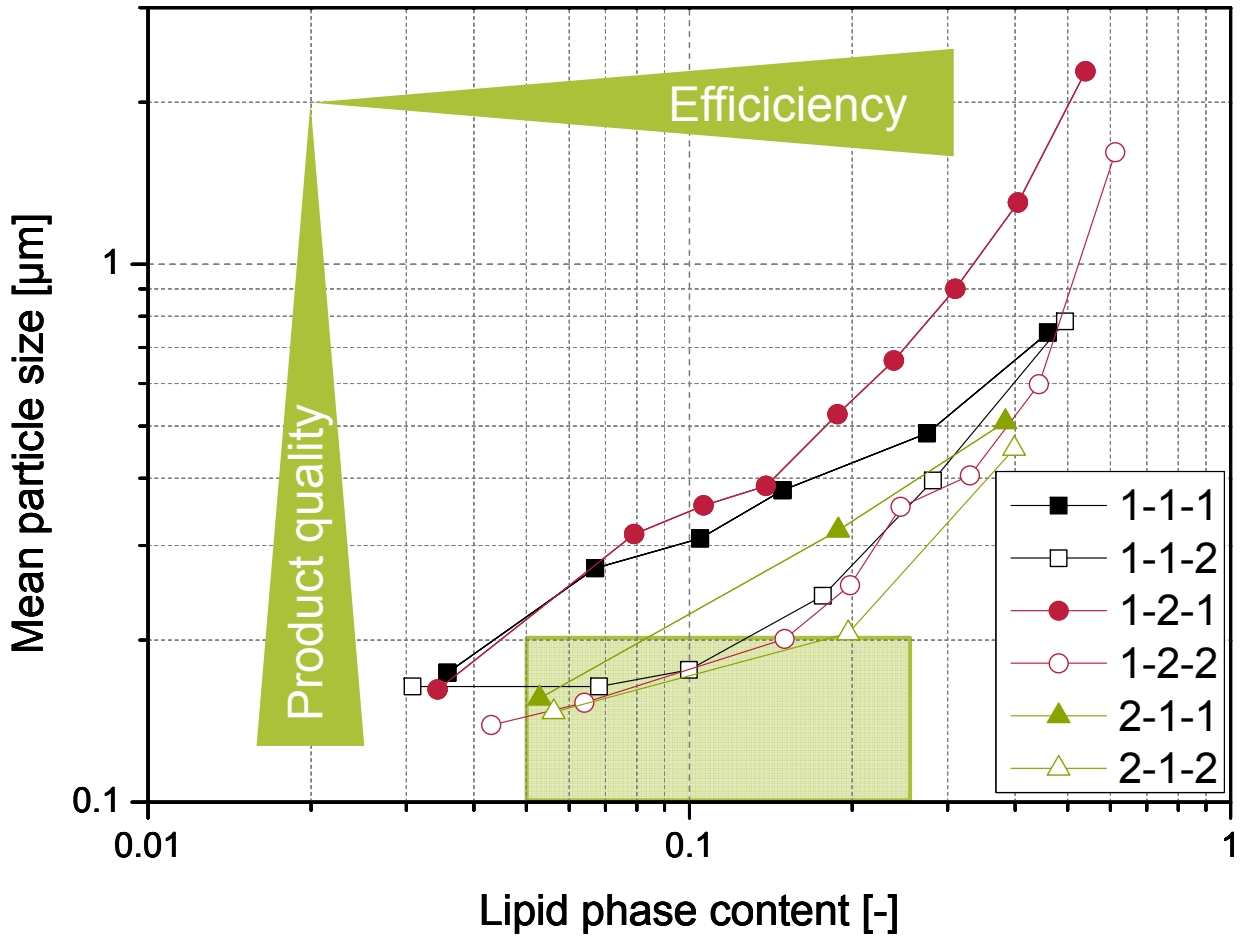


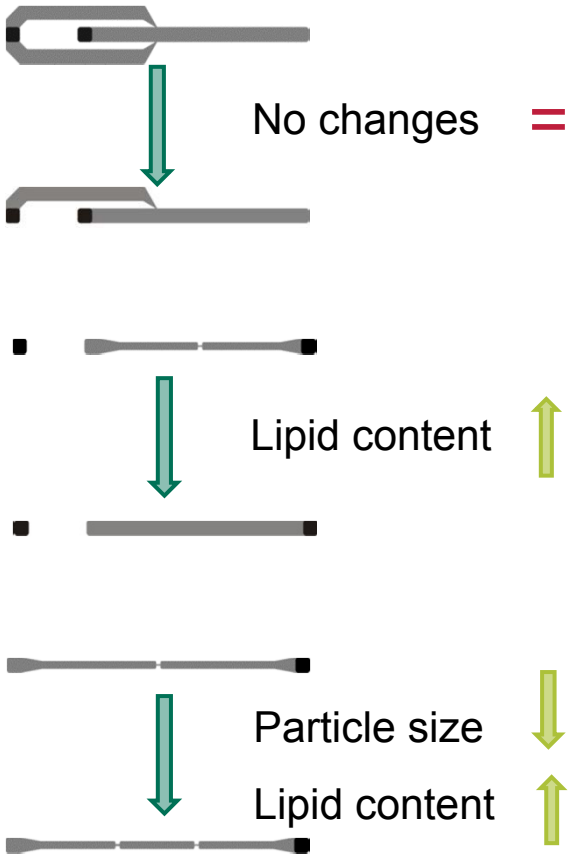
Δp = 200 bar p_C = 0 bar



Droplet – breakup mainly by turbulent stresses

Overall efficiency of integrated overall microsystem



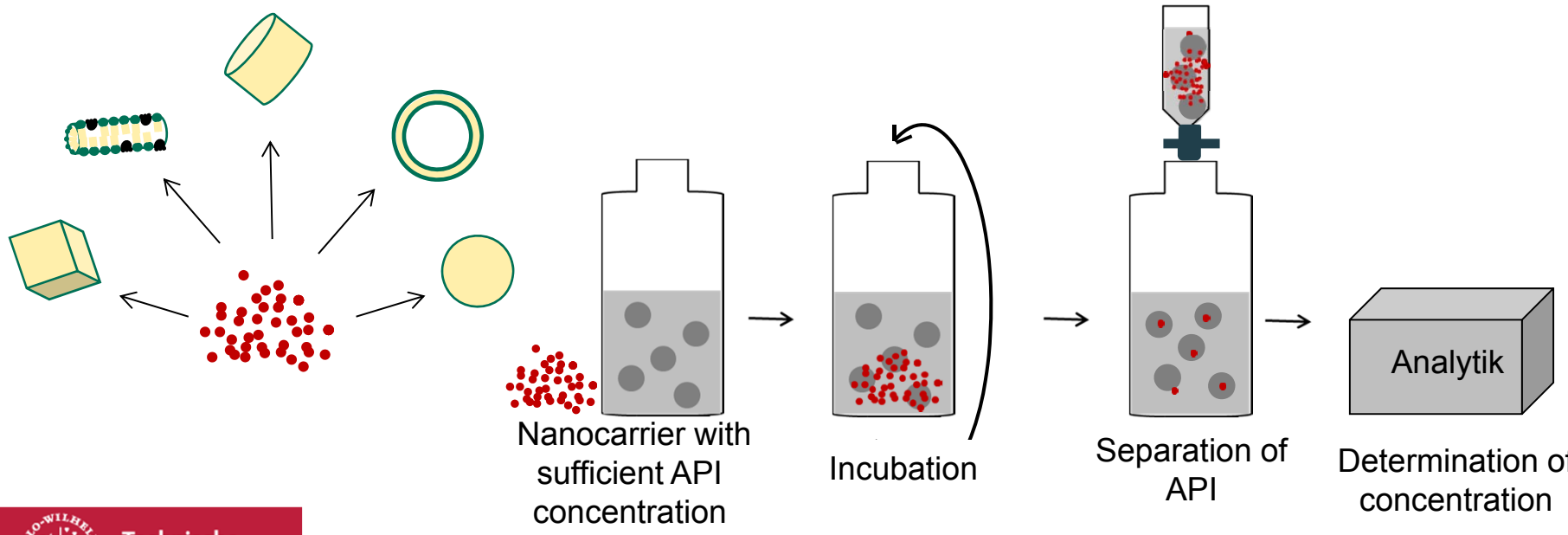


p_L = 1000 bar

Further Research (Heike Bunjes)
Lipid nano carrier as drug carrier

- Lipid nanocarrier as possibility to formulate poorly soluble API
- Many possibilites of variation and individualisation (lipid component, emulsifier, structure, …
- Today no rational choice of carrier – API – combination

⇨ Determination of appropriate carrier systems by new screening methods



Research example
Individualized orodispersible films (ODFs)

- Thin, polymeric films
- Disintegrate directly in the mouth
- Advantages for children, elderly and persons with swallowing problems

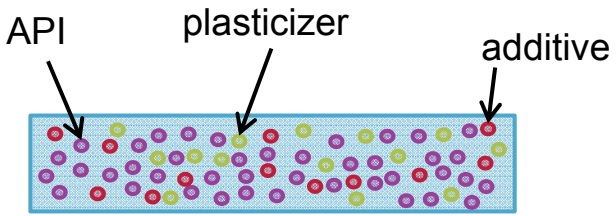
Water-soluble film-forming polymer

Active pharmaceutical ingredient (API)

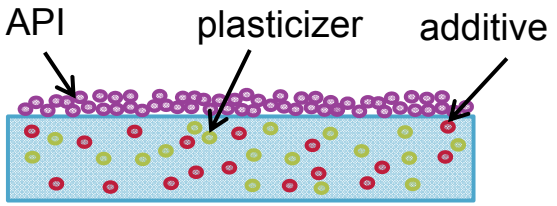
Plasticizer

Additives: fillers, colors, flavors

API containing ODF



API loaded ODF



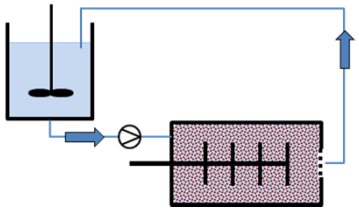
→ Personalization of dosage forms

Source: http://www.tesa-labtec.com

Loading of drug free ODF templates

Drug free templates

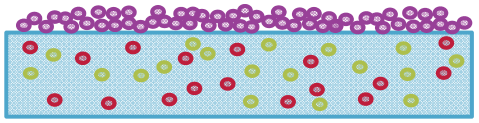
- Mixing of film forming polymer and additives
- Solvent Casting Method



Nanoparticulate suspension

- Milling of poorly water-soluble APIs
  → Improving Bioavailability
- Stirred media mill

Film loading

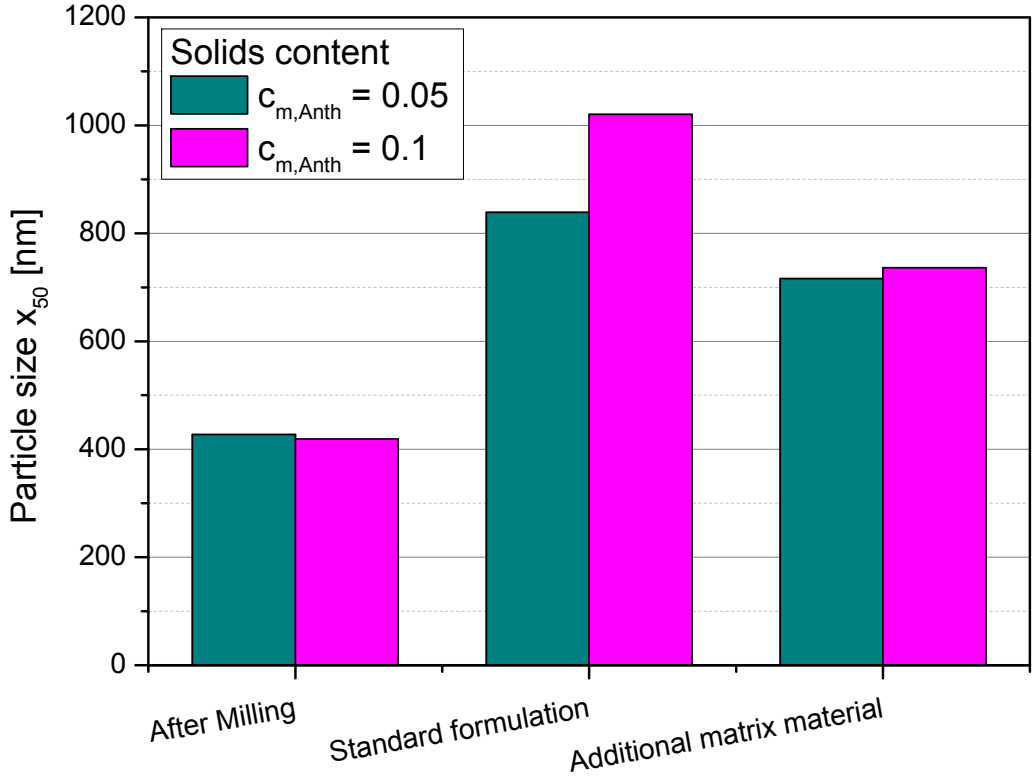


Loading a personalized API amount on top of drug free template

Particle size after film redispersion

Main target:

→ Preservation of particle sizes when redispersed in water



Additive: HPC

Standard formulation milling:

$c_{m,additive}$ = 0.25

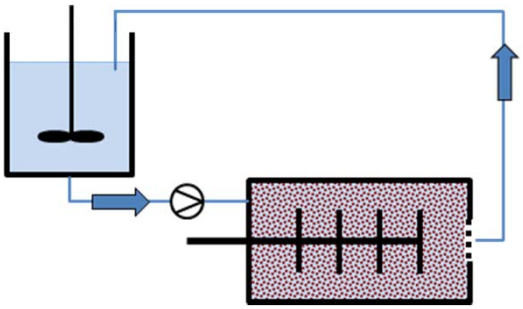
Additional matrix material:

$c_{m,Additive}$ = 0.5

→ Reduction of particle agglomeration due to increasing polymer amount

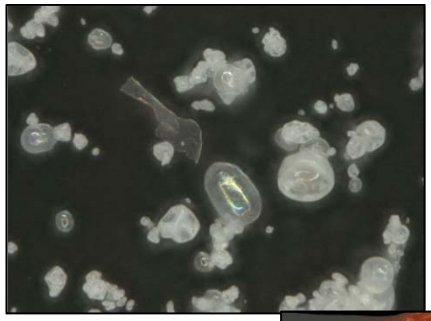
Instant ODFs

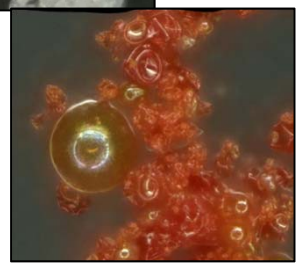
Personalization with nanoparticle loaded powders



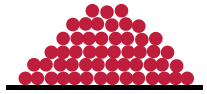
Processing in stirred media mill

1. Preparation of nanosuspension
2. Solving polymer
3. Homogenization



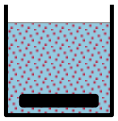


Spray drying



Standard manufacturing process

Storage of Powder



Redispersing powder in water

- Using different devices

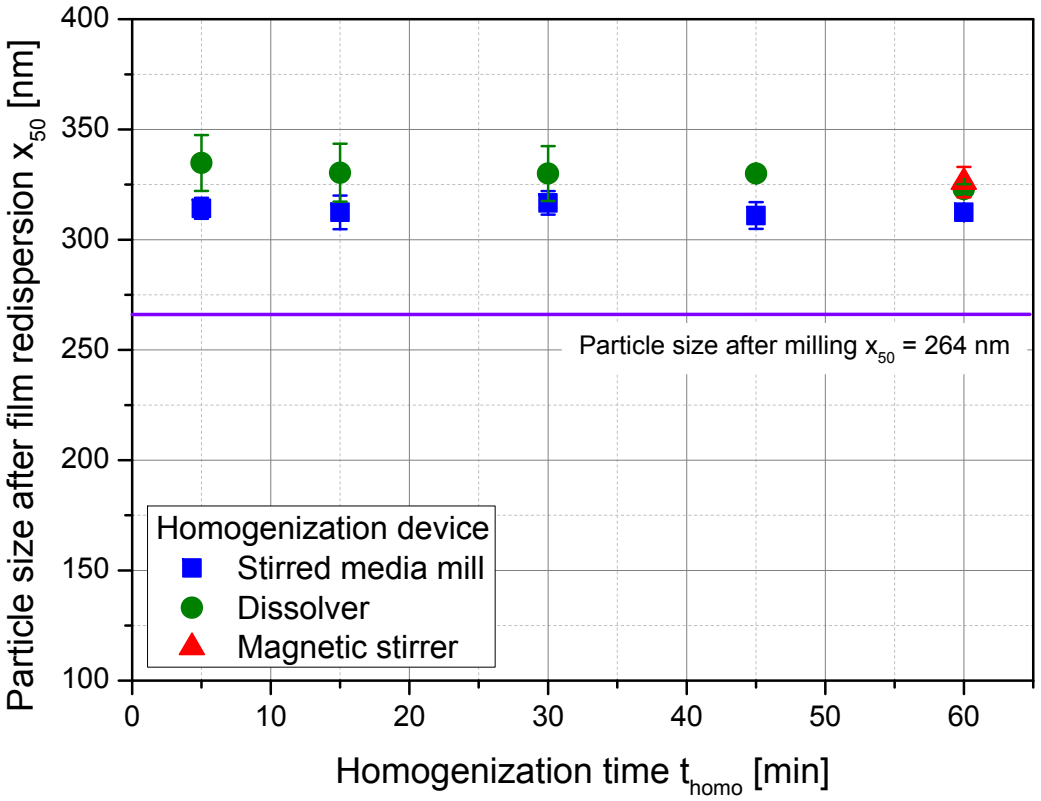
Degassing

Degassing

Solvent Casting

- Applicate suspension on substrate
- Evaporation of solvent

Influence of homogenization device



Stirred media mill:

- Smallest particle sizes are received

Dissolver:

- Reduction of particles sizes with longer times

Magnetic stirrer:

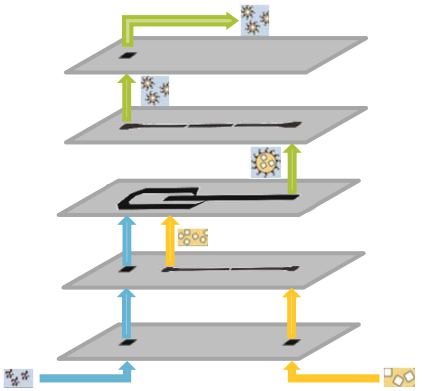
- **Sufficient** after longer stirring time of 60 min

→ No differences vs. Dissolver

Individualized processing of ODFs with one or more different API can be performed in pharmacies or hospitals

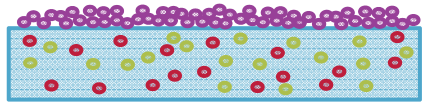
Conclusions

- Center of Pharmaceutical Engineering provides interdisciplinary knowledge and technology platform for the development of individulized medicine
- Main future objective of PVZ is how individualised and efficient medicine can be designed and produced with low costs?

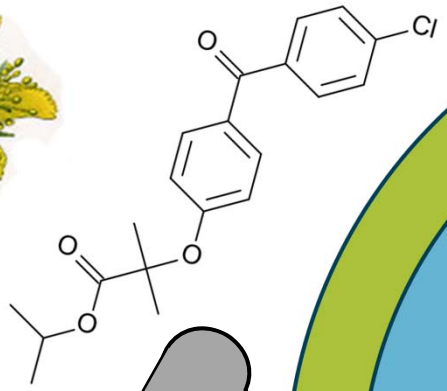


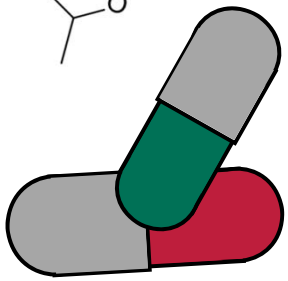
- Nanoparticulate drug carrier can be individually produced by microfluidic devices

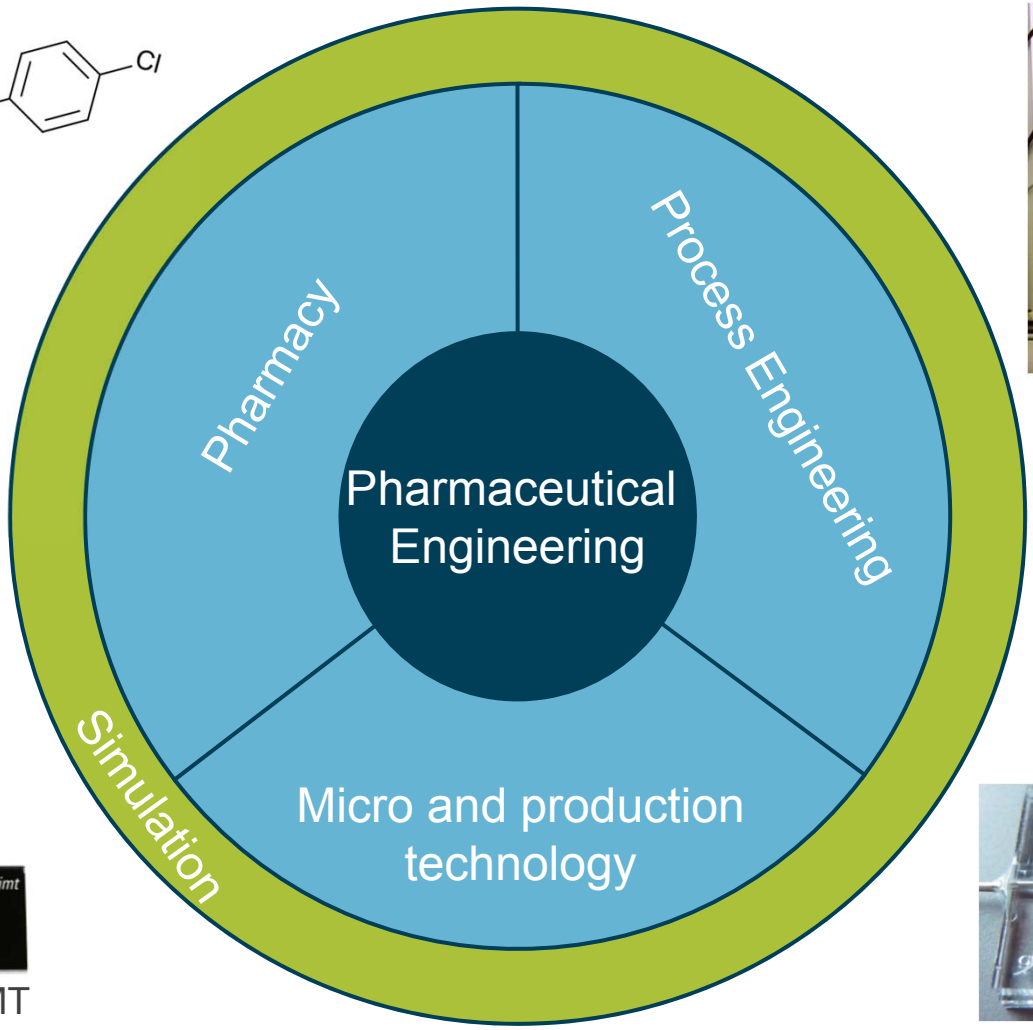
- Personalization of oral dosage forms is possible with ODFs
  1. Loading of APIs on drug free templates
     - Templates can be loaded with suspension
     - The amount of API can be adjusted
  2. Instant ODF powder

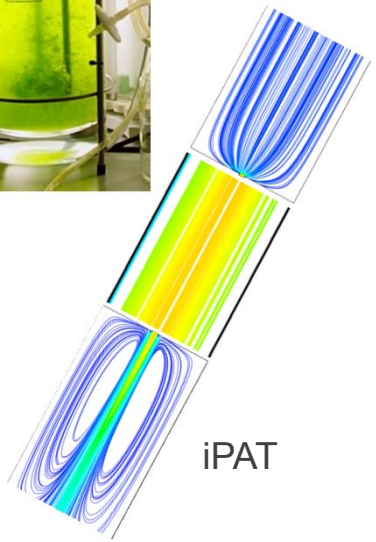


PVZ – Center of Pharmaceutical Engineerung
A unique combination of competencies in Germany









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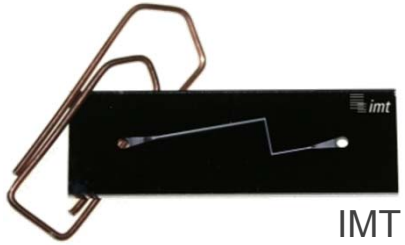

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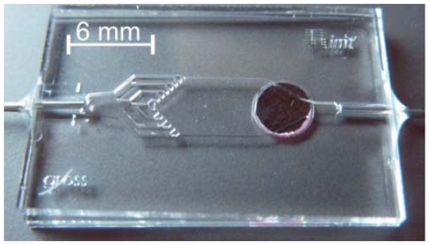
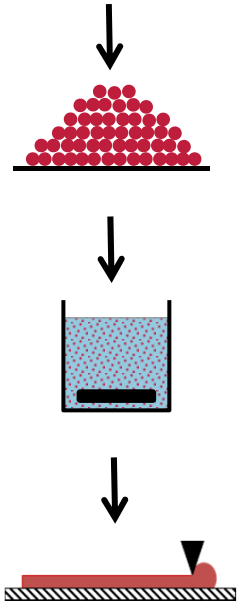


IMT, ibvt

Instant ODFs

Personalization with nanoparticle loaded powders



Advantages for the personalization of ODFs

- Production of powder in the industrial plants with set ratio API : Polymer
- Individualized processing of ODFs can be performed in pharmacies or hospitals
- Dosing by adding polymer and water to the Instant ODF powder during redispersion in water
- Combination of several APIs by homogenizing the different powders
  → Application of only one ODF