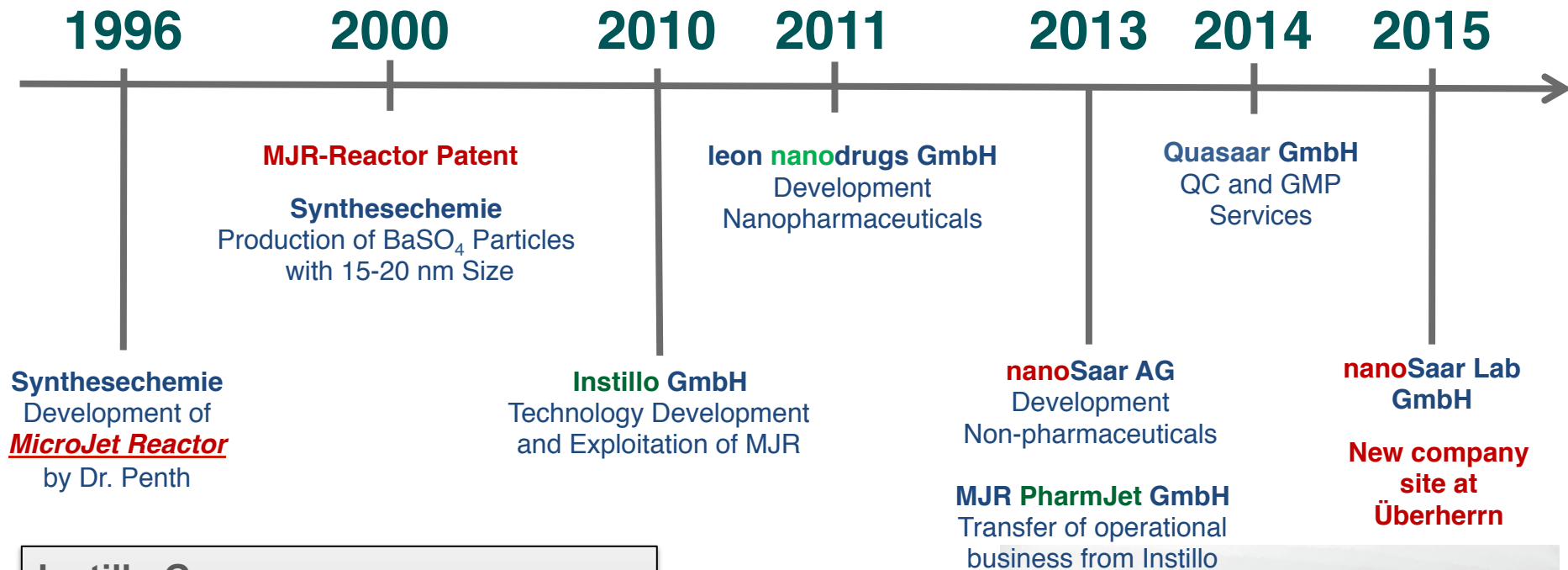


Instillo Group, Überherrn

**„Nano- und Mikropartikel an der
Schnittstelle zwischen Pharma und
angrenzenden Bereichen**

>20 Years of experience with Particles and Microreactors



Instillo Group

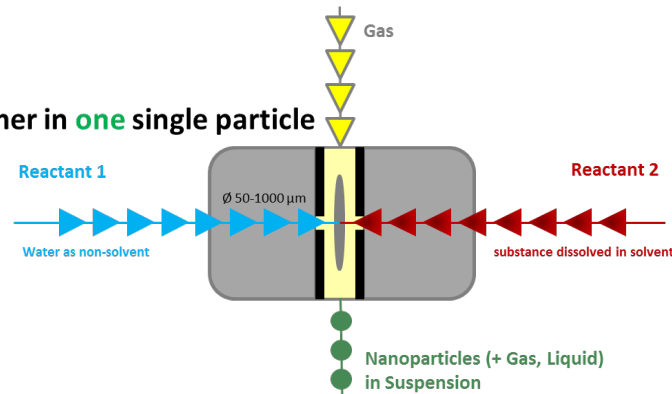
- >40 employees at Überherrn
- >10 employees at Munich
- 3 employees at Starnberg



- 12000 m² total area; 5000 m² premises
- 350 m² offices; 1000 m² laboratories (expandable)
- 500 m³ ICH-stability storage (expandable to 2000m³)

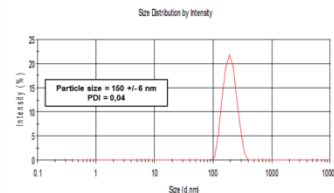
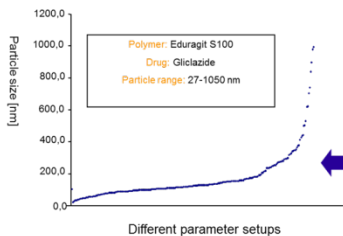
Unique features of Particles with Microreactors

1. **continuous** precipitation
2. **one-step** reaction
3. **no** toxic solvents if needed
4. combination of substance & polymer in **one** single particle



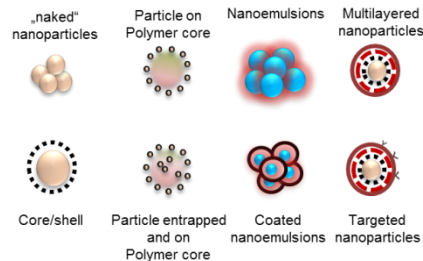
Simple, efficient and reproducible way to create nanoparticles

High quality Nanoparticles



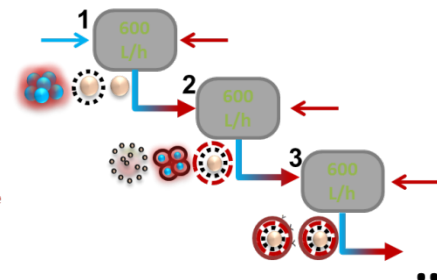
Homogenous particles (PDI<0.2)

Efficient control of the parameters for the desired particles



Production of complex systems

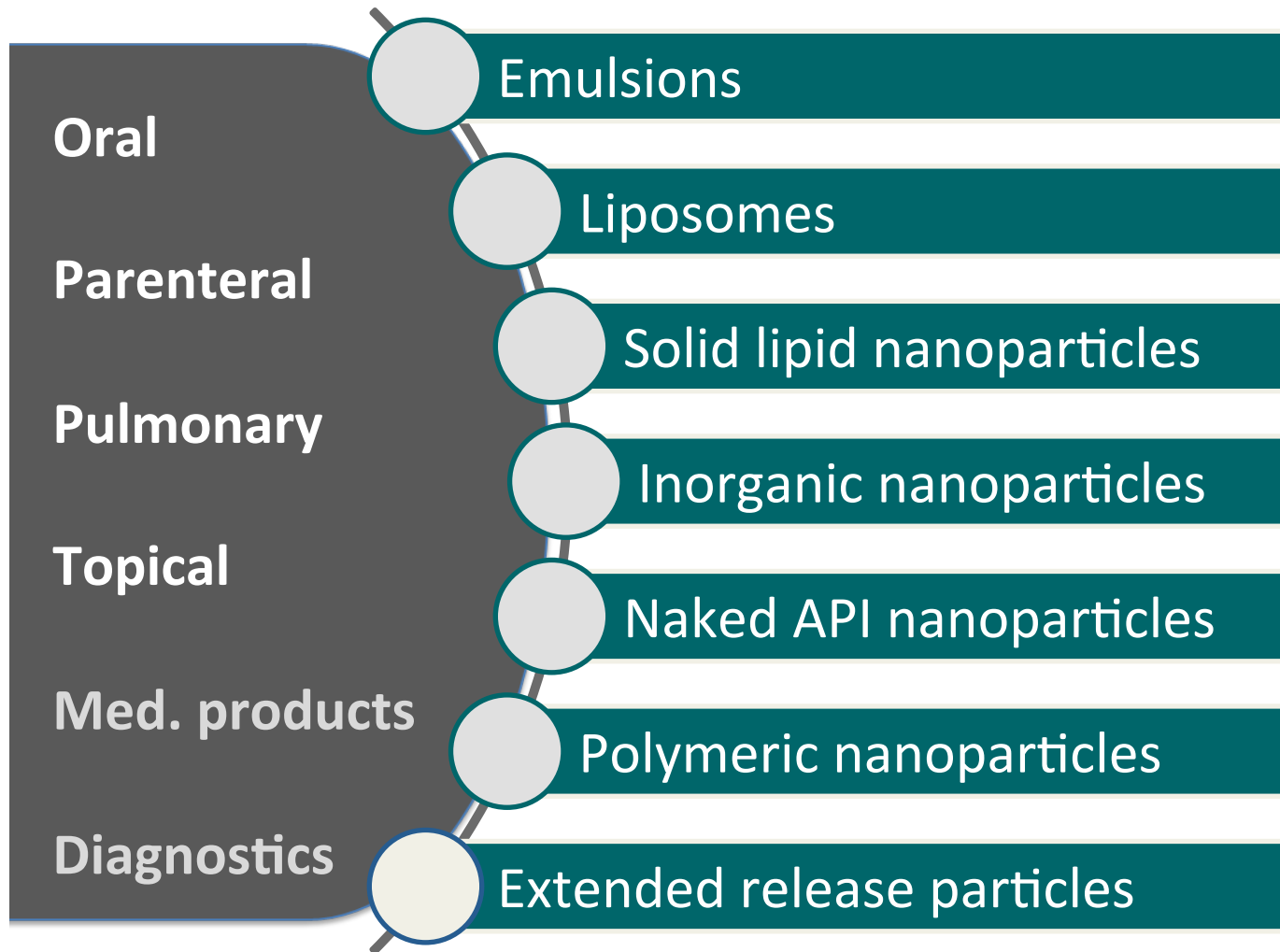
by Cascade-mode of MJR



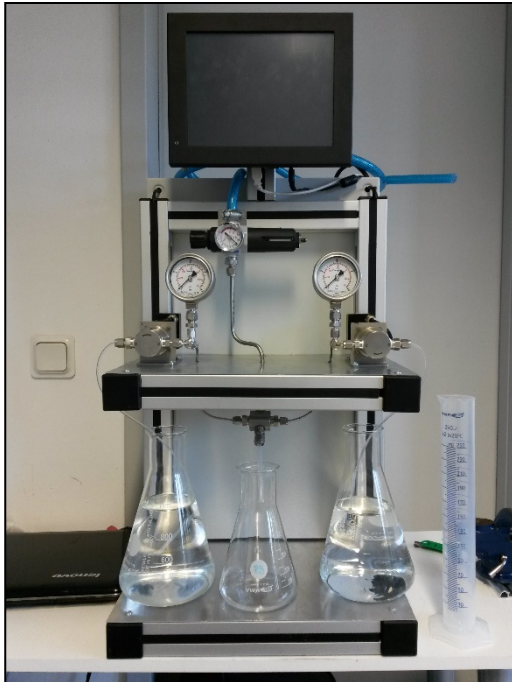
maximum throughput (Suspension):	600 l/h
Nanoparticles in Suspension:	10%
Production:	60 kg/h

High Throughput & easy Scale-up by numbering up

All around particles



From Lab Scale to Production Scale



Micro Reactor for R&D Lab



Micro Reactor for Small Scale Production (GMP)

Nanoformulations from R&D to GMP

Challenges to overcome:

- Particle range defined in regulatory guidelines ($>100\ \mu\text{m}$, absence of particles $>10\ \mu\text{m}$) does not cover state-of-the-art particle technology (10 nm – 1000 nm)
- Not all relevant methods / equipment for characterization of nanoparticles are established in GMP
- Thoroughly characterization of particles are important, because of great impact of particle characteristics on drug product performance, bioavailability and efficacy
- Need for own validation and qualification concepts or development of dedicated equipment!
- Long-term stability effects of particles must be evaluated (agglomeration, disintegration, leakage effects...)
- Toxicological effects of particles must be investigated / defined for technical particle size ranges



Development

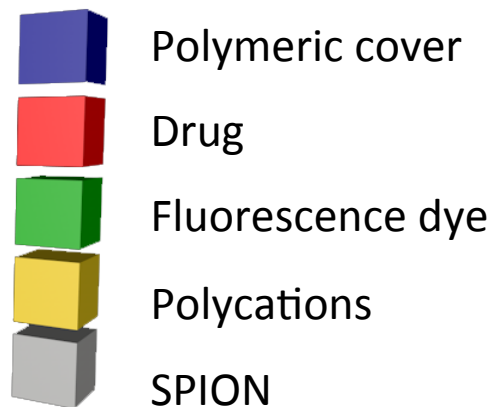
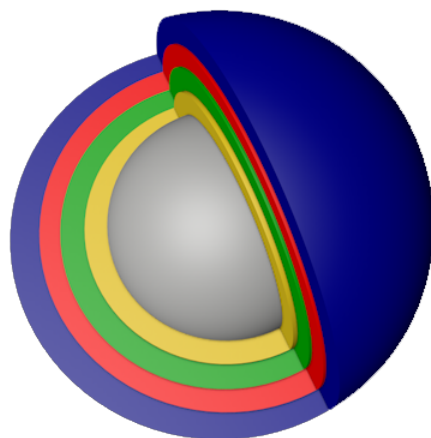


GMP

SPION can be used simultaneously

- As drug delivery vehicle
 - = > Moved by magnetic forces
- Control of particles at tumor side
- For Hyperthermia therapy

→ Combination of several therapies increases the patient compliance



Complex structure of SPION needed

Coating of SPION

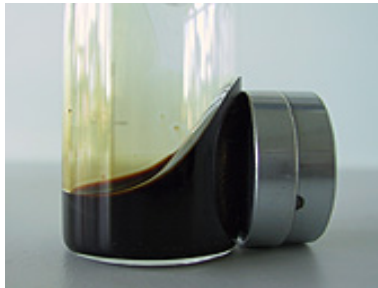
- Using various polyanions or rather polycations
- Using various silans
- Molecular imprinting

Functionalization of SPION

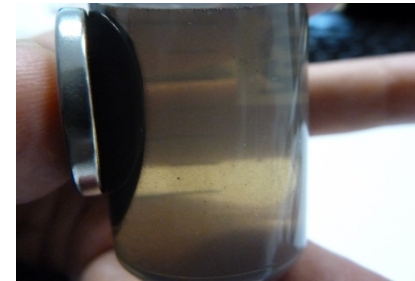
- Disintegration of polymeric cover
 - pH-dependent
 - Temperature- dependent

In-vitro diagnostics with magnetic nanoparticles

Ferrofluid



Nanoferrit



Advantage of magnetic nanoparticles

- Easy visualisation by MRT or EM
- Moving of particles in magnetic field (lab on a chip)
- Easy separation of particles by magnetic field
- Easy quantification of bound substrate by Magnet-Relaxometry

Advantage of Microreactor method

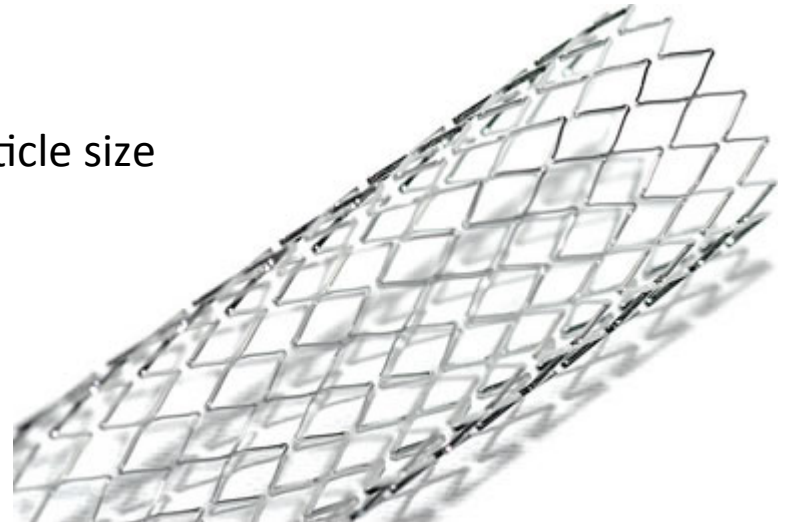
- High volume production of controlled particle size
- Coating with various surface agents possible
- Functionalisation of surface with various molecules possible

Advantage of polymeric nanoparticles

- Homogenous coating of stents
- Extended release of API
- Controlled application of API
- Optimal API dosing
- Enhanced stability

Advantage of Microreactor method

- High API loading into polymeric systems
- Homogenous release through homogenous particle size



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