TNO innovation for life

LEIDEN DRUG DEVELOPMENT CONFERENCE

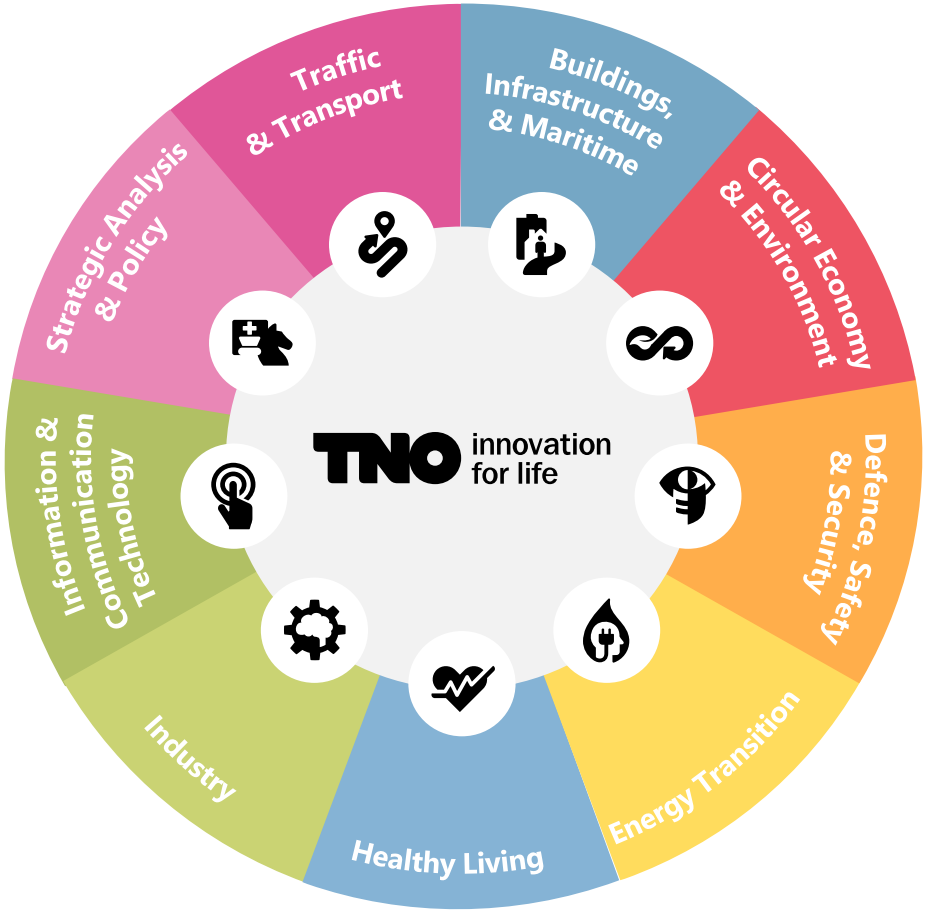
3D PHARMA PRINTING @ TNO

KJELD VAN BOMMEL

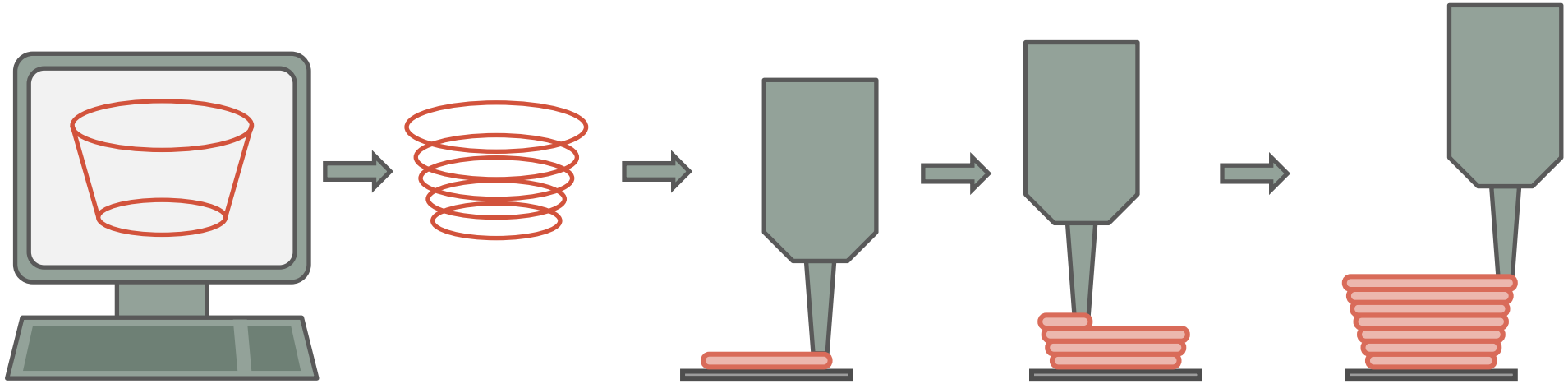
LDDC – September 27, 2022

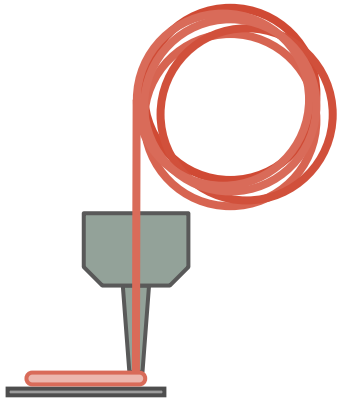
TNO
WHO WE ARE AND WHAT WE DO

- Largest independent contract research and innovation organization in The Netherlands, est. 1932
- Over 3400 researchers active in 9 Units
- Positioned between universities and commercial companies
- **Mission:** Apply scientific knowledge to boost the innovative strength of our partners
- *Active in the 3D printing space for 30+ years*

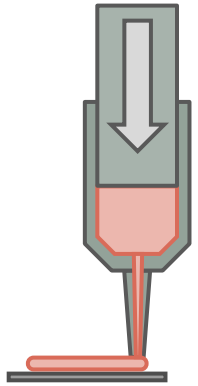


3D PRINTING
OVERVIEW OF TECHNOLOGIES





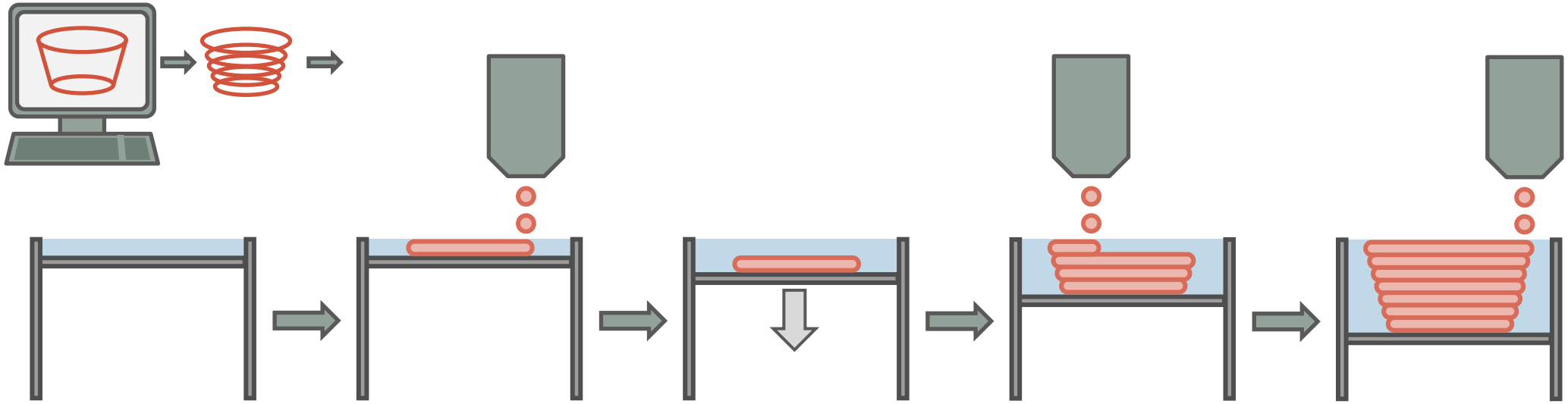
Fused
Deposition
Modeling

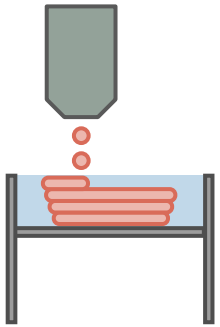


(semi solid)
Extrusion
Printing

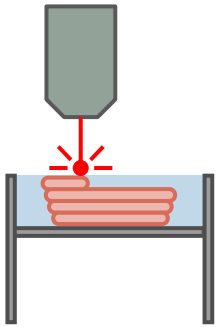
3D PRINTING
EXTRUSION PRINTING

3D PRINTING
OVERVIEW OF TECHNOLOGIES





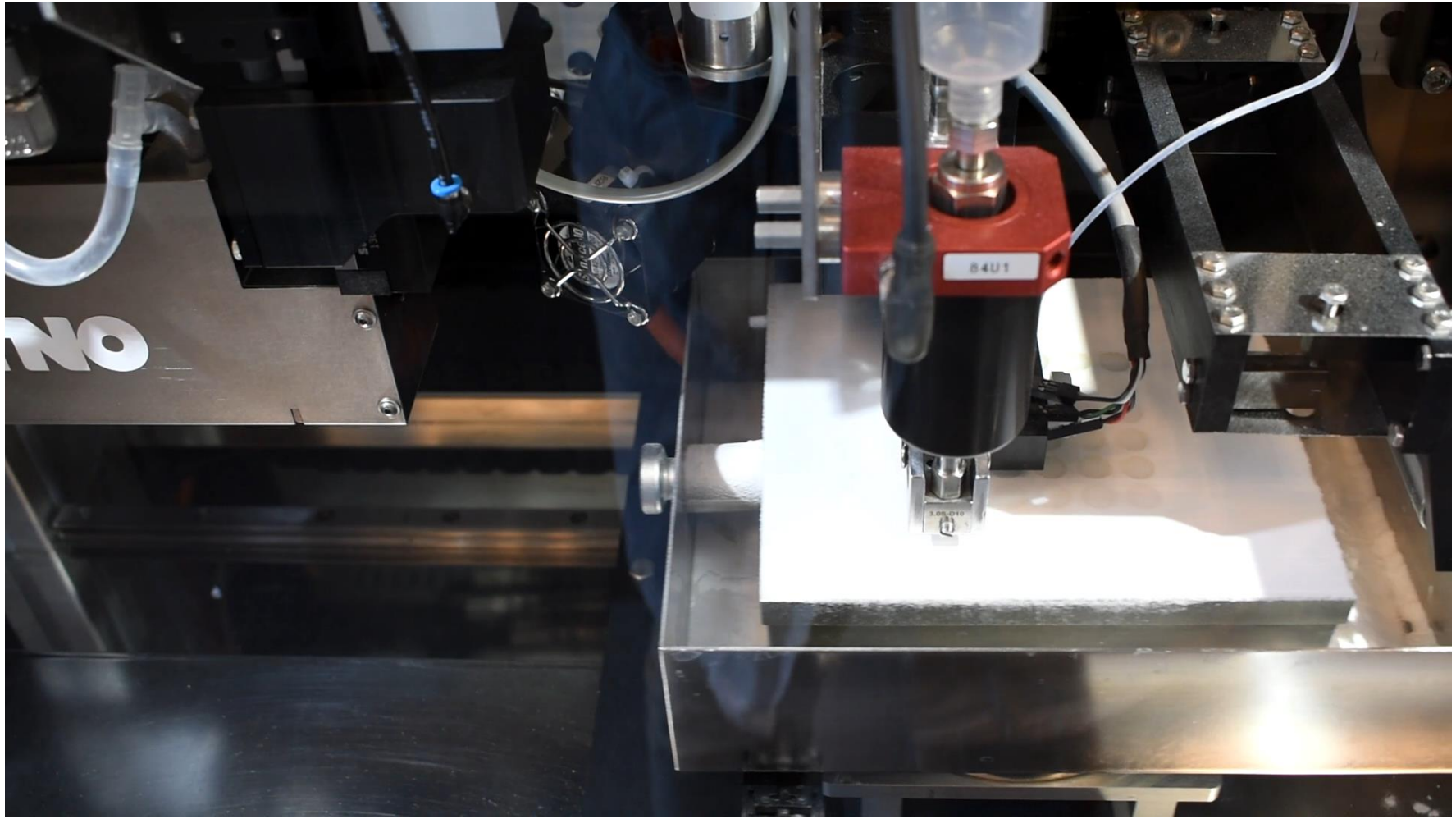
Powder Bed Printing



Selective Laser Sintering

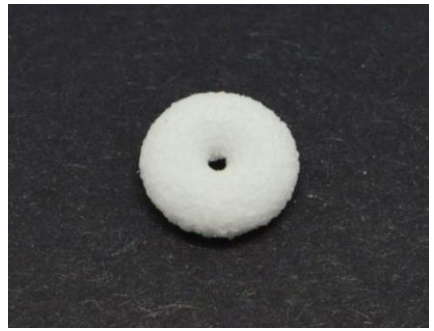
3D PRINTING

POWDER BED PRINTING + SELECTIVE LASER SINTERING

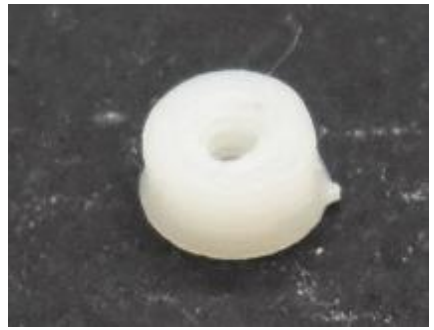
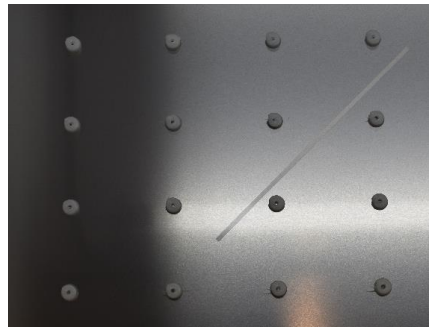


3D PHARMA PRINTING
PRINTED TABLETS (TNO)





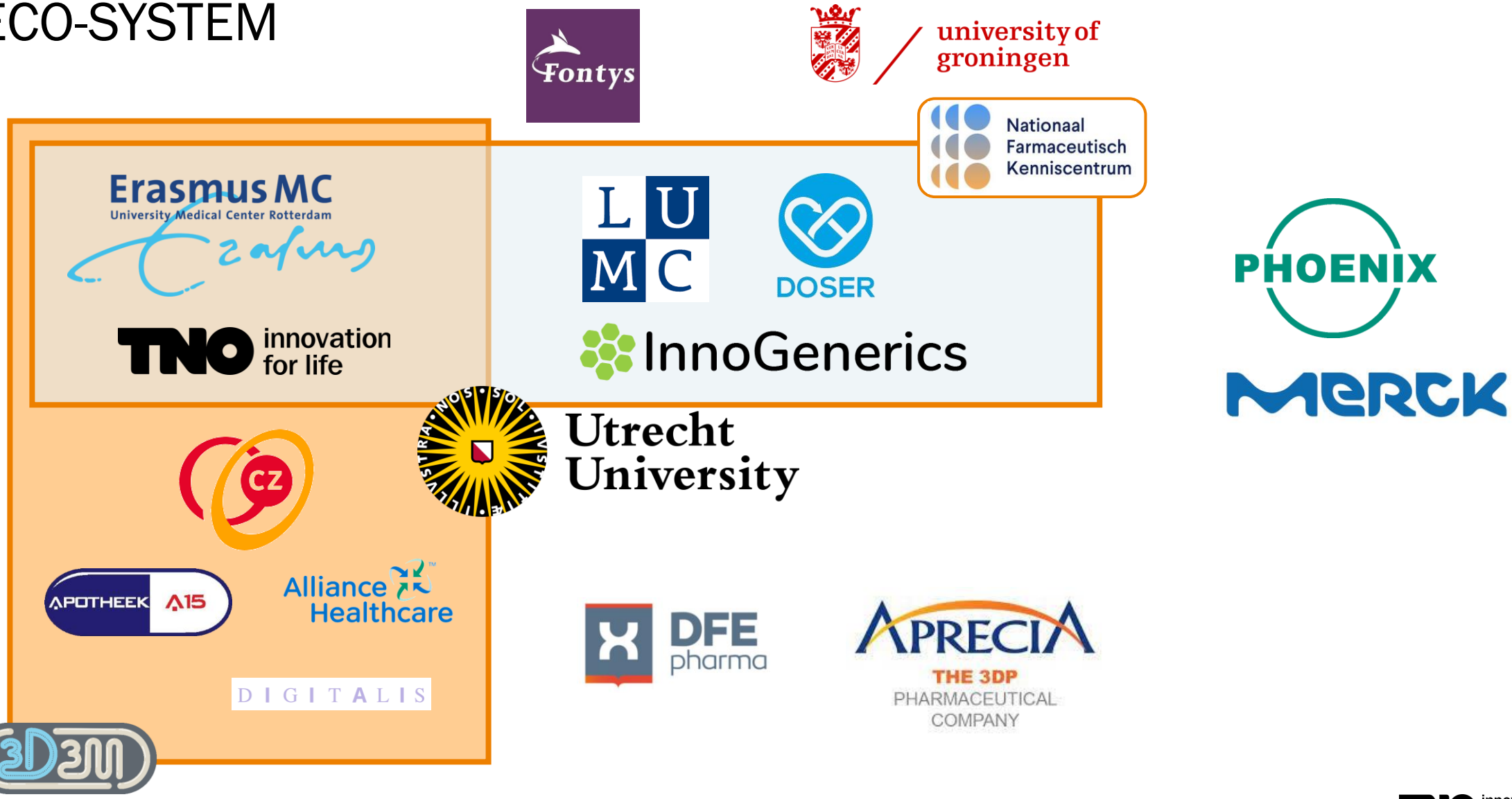
3D PHARMA PRINTING

USPs

- **Research & Development tool**
  - Quickly produce and screen new formulations, shapes, dosages, release profiles, …
  - Printing ON medical products – e.g. conformal deposition on implants
- **Personalized medication**
  - API dose tuned to the need of the individual patient – including children's medication
  - Polypill – combine multiple APIs to decrease pill burden
  - Creation of specific dosing regimes – slow in- or decrease of API over time
- **Different logistics**
  - Local and on demand production
  - Creation of small batches
  - Less stability issues (?)

3D PHARMA PRINTING @ TNO

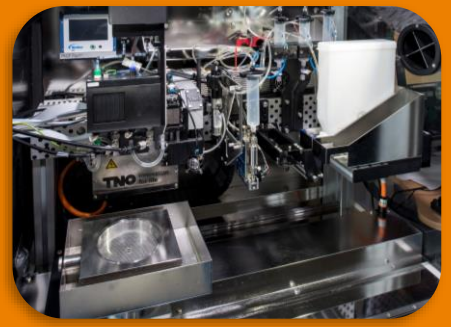
ECO-SYSTEM



3D PHARMA PRINTING @ TNO
PROPOSITIONS

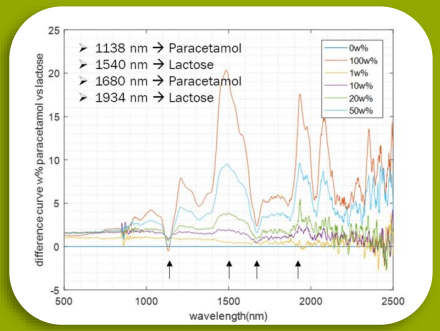
Feasibility studies

Next generation equipment development



Printing of personalized medicine

Non-destructive validation

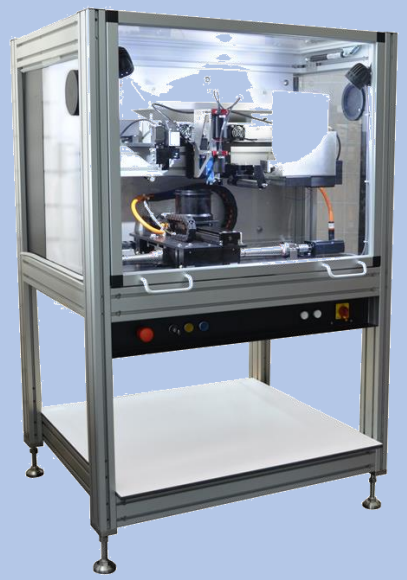


NEXT GENERATION EQUIPMENT DEVELOPMENT
TECHNOLOGY PLATFORMS DEVELOPED BY TNO

High accuracy
Extrusion printing

High speed, high power
Extrusion printing

Up-scaling
Technologies



Powder bed printing and
Selective laser sintering
(separate or combined)

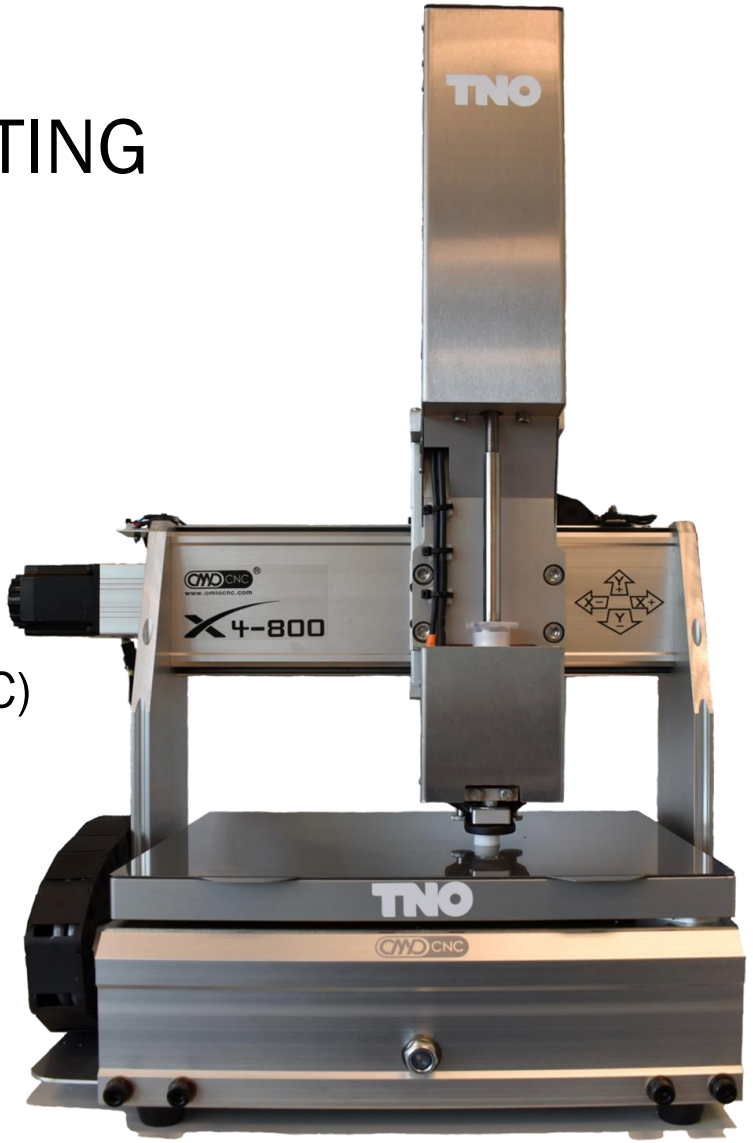
TECHNOLOGY PLATFORM

HIGH ACCURACY (LOW MELT) EXTRUSION PRINTING

Focus: high accuracy for small tablets (e.g. paediatrics)

- Stiff print head and syringe construction
- Stainless steel syringes / aluminum nozzles
- Smaller step size for extrusion motor
- High accuracy temperature control for syringes and nozzles (+/- 0.1°C)

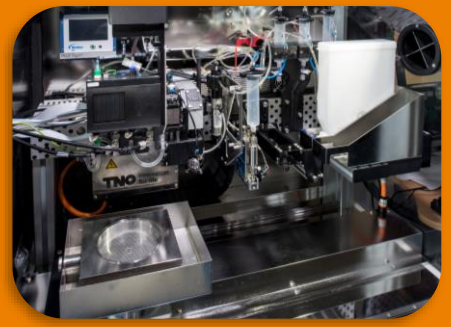
- *Powerful extruder with monitoring of extruder force*
- *Print speed up to 3000 mm/min*
- *Integrated cooling air shower, adjustable in air temperature and flow*
- *Print bed can be heated, levelled, and switched out*
- *Easy to clean*



3D PHARMA PRINTING @ TNO
PROPOSITIONS

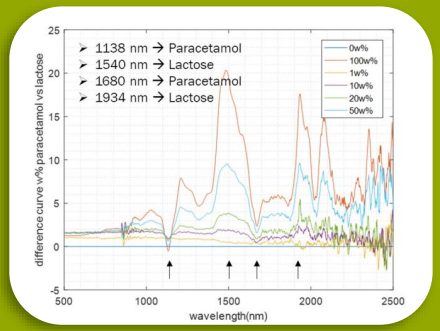
Feasibility studies

Next generation equipment development



Printing of personalized medicine

Non-destructive validation



Current situation

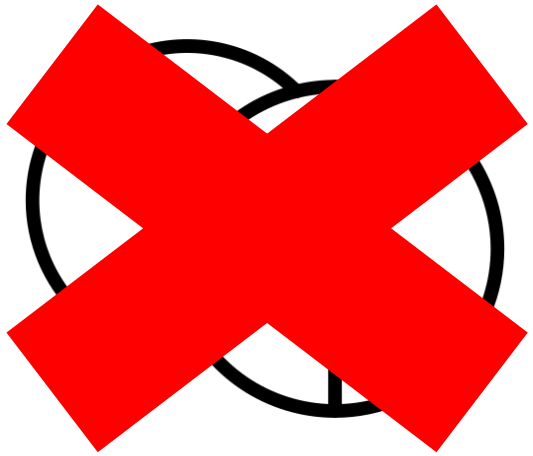
Manipulating drugs needed in **>50%** of drug administrations in children

crushing tablets	making suspension
taste masking	splitting tablets
opening capsules	using iv fluids orally
diluting solutions	cutting patches

A.vd Vossen et al. Acta Pediatrica 2019 108, 1475 – 1481.

Slides courtesy of Elisabeth Ruijgrok, PharmD, PhD
Pediatric Clinical Pharmacist, Deputy Head of Clinical Pharmacy

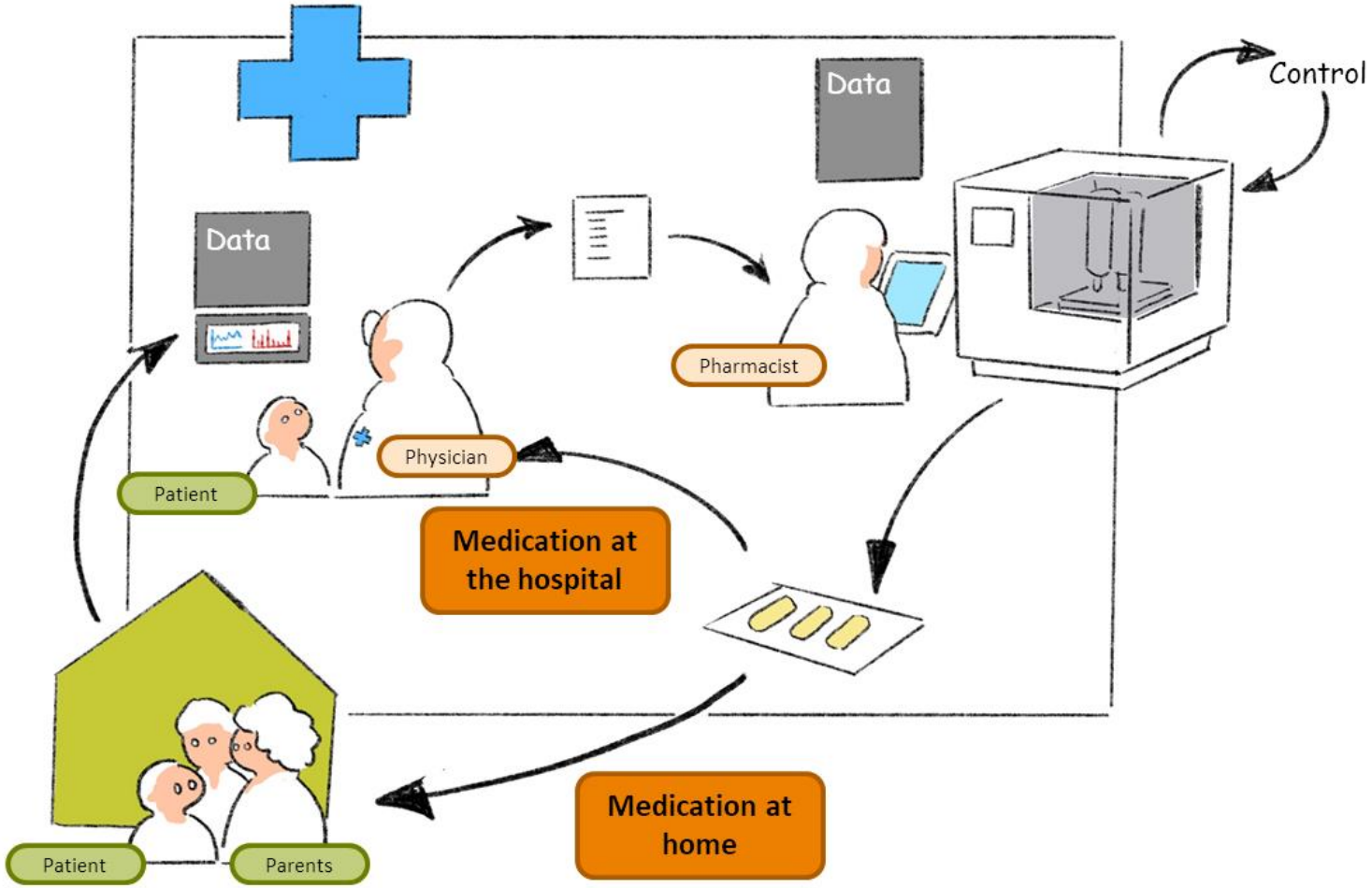
Flecainide 4.2 mg



Tablet 50 mg?

Drug manipulation

PRINTING OF PERSONALIZED MEDICINE
COLLABORATION ERASMUS MC

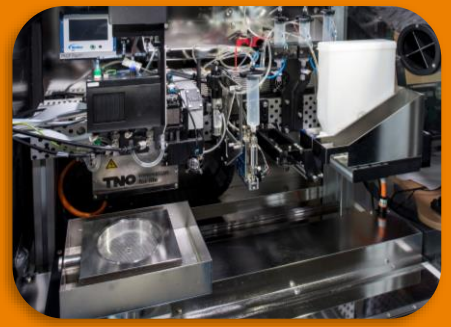


afe and affordable production of tailor made medication for individual patients by developing technological automated production either in the hospital or in decentralized locations.

3D PHARMA PRINTING @ TNO
PROPOSITIONS

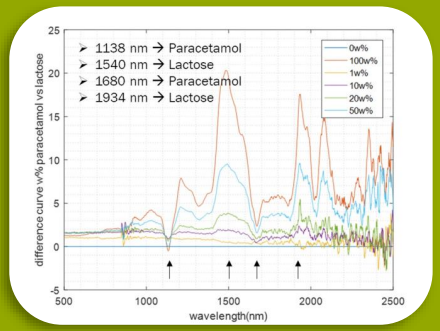
Feasibility studies

Next generation equipment development



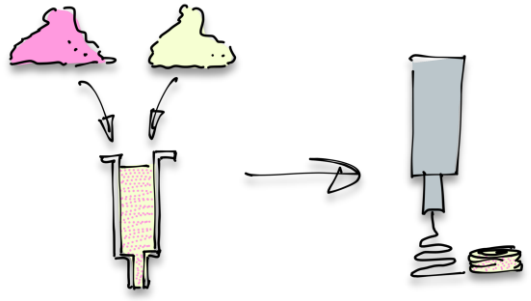
Printing of personalized medicine

Non-destructive validation



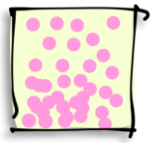
NON-DESTRUCTIVE VALIDATION
TABLET QUALITY - HOW TO VALIDATE?

- When producing ever smaller series of tablets destructive testing will be no longer a valid solution.

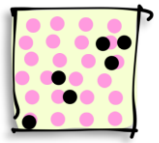


Which API?
API dose?

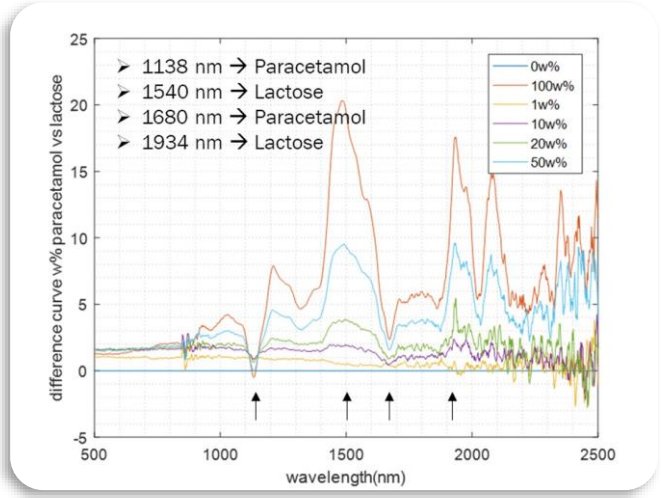
API dose = Tablet weight x API % in bulk



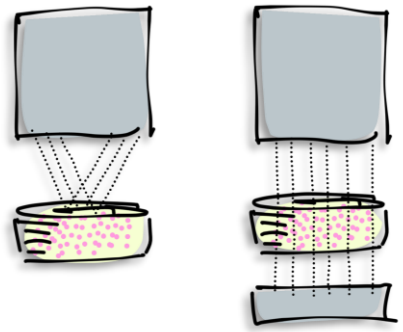
If: No inhomogeneity



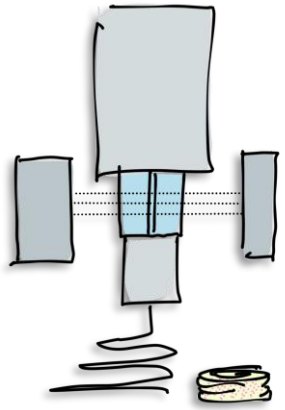
If: No API degradation



Spectral analysis



Look at tablet

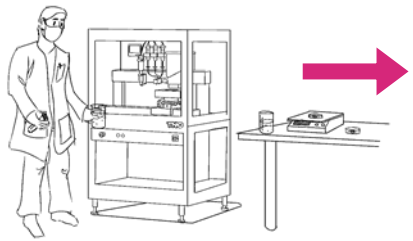


Look at filament

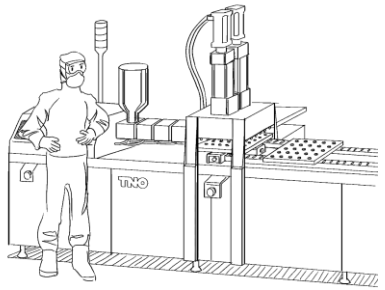
3D PHARMA PRINTING
ROADMAP

Pharma

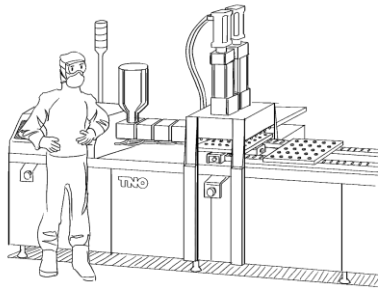
PHARMA R&D



PHARMA R&D FLEXIBLE PRODUCTION

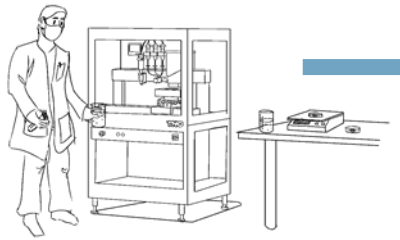


PHARMA FLEXIBLE PRODUCTION

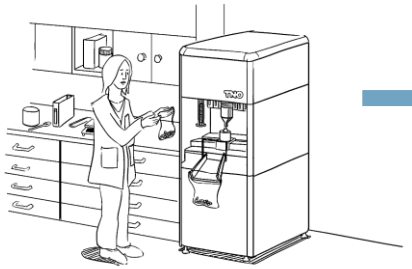


Hospital

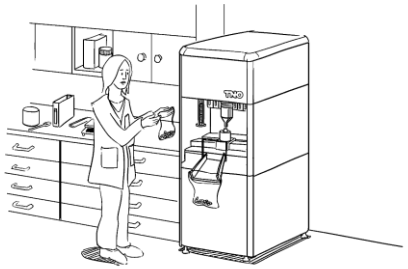
HOSPITAL PHARMACY R&D



HOSPITAL PHARMACY PERSONALIZED MEDICINE



GENERAL PHARMACY PERSONALIZED MEDICINE



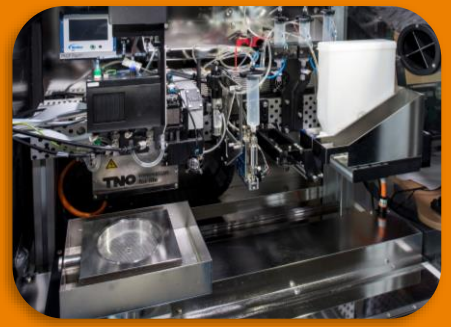
TIME

3D PHARMA PRINTING @ TNO

OPPORTUNITIES TO COLLABORATE

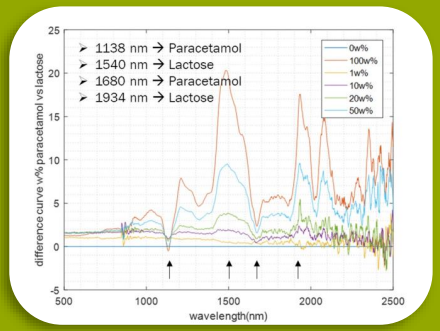
Feasibility studies

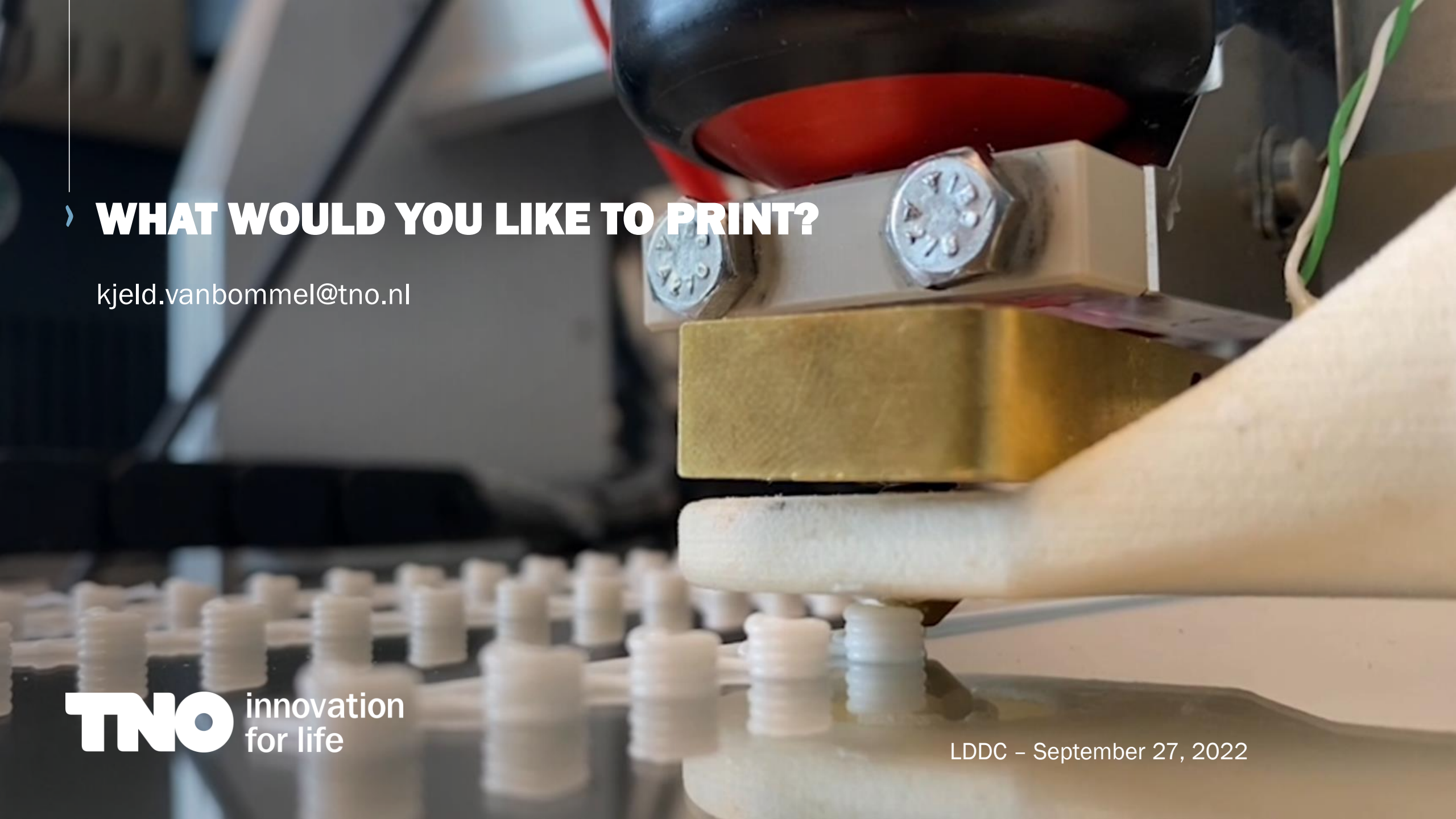
Next generation equipment development



Printing of personalized medicine

Non-destructive validation





WHAT WOULD YOU LIKE TO PRINT?

kjeld.vanbommel@tno.nl

TNO innovation for life

LDDC – September 27, 2022