

Options to implement digital printing of medicines in clinical practice



Veldhoven, 30.3.2022

We personalize Healthcare

Personalized drugs from 2D and 3D FlexDosePrinter



From Technology to Business

One size fits all vs individual size

- 3DP, like 2DP, enables very efficient production of *relevant pharmaceuticals* and/or for *special populations*.
 - Relevant API:
 - **API** with narrow therapeutic Index, direct feedback control, therapy-limiting ADEs, etc.
 - Special population:
 - Children (rapidly changing organ function, commercially unavailable API, etc.)
 - Geriatric patients (dysphagia, adherence challenges, polypharmacotherapy, etc.)
- ➔ If we want to put the patient at the centre of care and use the efficiencies of the 3DP and 2DP, then individual size makes sense.
- ➔ If it is purely about efficient manufacturing methods, then it will be about a technology shift in mass production.

Personalized tablets lead to improved therapy

Today's therapy with tablets and capsules is medically ineffective, inefficient & unnecessarily expensive.

The challenge:



- 60% of the prescribed drugs: not the desired therapeutic **benefit**



- Approx. **500,000 hospitalizations** in Germany and approx. 50,000 deaths in Germany due to inadequate drug therapy



- Silverager: up to **15 tablets** daily | in D more than **15 million people** take more than **3 tablets** daily



- Approx. 75% of all people in the western OECD countries over 65 years suffer from at least 1 chronic disease | Costs for **non-compliance** in Germany 10 billion €/year, in USA approx. 300 billion US \$

NON-COMPLIANCE

Personalized tablets enable tailored therapy:



- Improved therapy** | Fewer side effects | Better QoL



- Reduction of unnecessary **costs** for the health care system



- Avoidance of **supply bottlenecks**



- Massive reduction of **pharmaceutical waste**



- Share of tablets and capsules in the pharmaceutical market | **67%**



The solution: Digitally printed (2D/3D) personalized tablets

Digital Healthcare

Digitization is changing the healthcare markets | Patient centered and Physician driven process



The system is the basic prerequisite: hardware, software & pharma

The solution is digital | Projects on patients start in 2021 and 2022 | Printing is digital, local and on demand



Printer | Inks | Filaments | Software

DiHeSys has developed the FlexDosePrinter, which can digitally print personalized medications in 2D and 3D printing processes in pharmacies and hospitals. DiHeSys develops and supplies all the necessary components :

- Pharma Printer: FlexDosePrinter
- Inks containing active ingredients | **2D**
- Filaments containing active ingredients | **3D**
- Software

The **DiHeSys** system is GMP compliant and fully digitally integrable. Legal framework: formulation. **Drucker stht in der**

Rezeptur

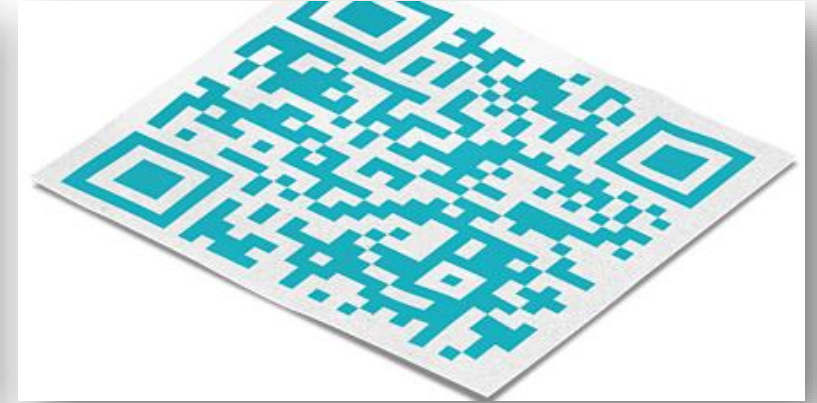
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3D Printing | Filaments

With 3D-printed tablets, the individually required drugs can be printed in a tablet in the dose required in each case. Time-dependent kinetics can be realized.

- One tablet
- One patient
- Once daily
- Exactly in the required dose



2D Printing | Inks

With 2D-printed tablets, medications can be easily combined individually and always with the correct single dose.

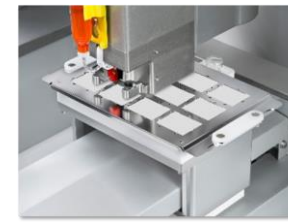
The imprint of the active ingredient as e.g. QR code enables further digital features. Limited to 40mg and no time delayed effect, but very easy to use.

First international projects have started with 2D-printed tablets.



Some concrete examples

Polypharmacotherapy | Organ Dependence | frequent dose changes



Pediatrics

Indication/API

Enalapril, Ramipril, Captopril, Methylphenidat, Sildenafil, HCT, Propranolol, etc.

Rationale & Approaches

No suitable dose available, dose adjustments necessary



Geriatrics

Polypill, polypharmacy, Antihypertensive API, CSE-antagonists, AT-antagonists, analgesics, Incontinence, etc.

Individual API, renal dysfunction, adherence, avoidance trash



Neurology

M. Parkinson, MS, Epilepsie **Ropinirol**, Entacapon, Levodopa, Carbidopa, THC, DMF, etc.

Individual API combination, **frequent dose adjustments**



Cardiology

Anticoagulation: Phenprocoumon, DOAC, Warfarin, etc.

Individual dosing, adherence, avoid drop-outs, waste avoidance.



Immunsuppression

Ciclosporin, **Everolimus**, Sirolimus, Corticosteroids, **Tacrolimus**, etc.

Blood level measurement necessary; dose to be adjusted individually, adherence, avoidance of waste, **PK study, Study for registration**



NTI

Anti-Cancer-Drugs, Tyrosine-Kinase-Inhibitors, Virustatics, CNS drugs, narcotics, TDM drugs, etc.

API specific, **bioavailability, drug trial**, individual low therapeutic window, avoid drop-outs.

Drug Trial: Cabozantinib

From setting to patient use

Medical need first



Selection Medical Need

- First step: integration medical professionals
- Inks and filaments are formulation drugs
- Supply network depending on use: outpatient and/or inpatient
- Besides physicians, also pharmacists and payers



Development system

- Development of active ingredient-containing ink (2D) and/or active ingredient-containing filament (3D) by DIHESYS/GenPLus
- Parallel adaptation software and printer. Customer demand, integration in Software Systems, IT Structures
- Qualification



Patient use

- After development and qualification, use on the patient takes place
- Inpatient as well as...
- ...outpatient. In addition to standard care, selective care is also available here.
- Filament/Inks by DIHESYS Wholesale/Partners

From science to business: What are possible options?

Potential concepts and approaches

Standard- or selective care models:

- Dependence on the respective **health care system** and especially on the **reimbursement mechanisms**.
- Decision of the setting: outpatient and/or inpatient.
- Use in daily practice: Which framework is possible de jure in which system.
- In social security systems (outpatient care) for example, **selective contracts**.
- Real world data/real world evidence approaches.

Drug trials, clinical studies

- In- and outpatient studies feasible
- Different studies and designs (i.e. bioavailability, phase 1 – phase 4, postmarketing)
- Different sponsors can be used here (pharmaceutical industry, university research budgets or national or international research funds).



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