Innovation policy for distributed innovation models in healthcare

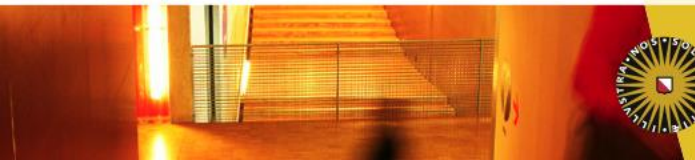
Wouter Boon & Ellen Moors

Eu-SPRI Conference 2018

Universiteit Utrecht

Grand societal challenges

- Grand societal challenges approached with alternative innovation models
- Considering demand-side policy is important (Boon & Edler, 2018)



Distributed innovation

- One alternative innovation model is distributed innovation
- Rise of distributed, innovative communities: community-supported agriculture, DIY gene editing, 3D printing hubs
- We heard about the self-regulated, policy experiments, etc.

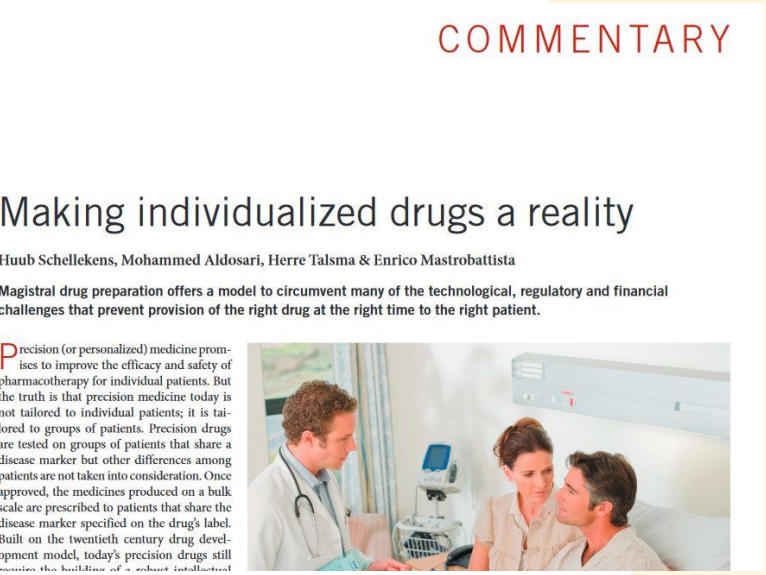
Innovation policy issues

- No support for user innovators
- Market failure in diffusing user ideas
- User ideas are contextualized
- Relation to intellectual property and stimulation of innovation
- Relation to quality standards
- Formation of markets

→ Market and system failures

Exciting distributed project…

- ‘Proof of principle’ pilot on high-tech solution for local production of an enzyme replacement therapy in an academic medical hospital
- Principal roles for medical specialists, hospital pharmacists
- There are technical, institutional and ethical challenges



COMMENTARY

Making individualized drugs a reality

Huub Schellekens, Mohammed Aldosari, Herre Talsma & Enrico Mastrobattista

Magistral drug preparation offers a model to circumvent many of the technological, regulatory and financial challenges that prevent provision of the right drug at the right time to the right patient.

Precision (or personalized) medicine promises to improve the efficacy and safety of pharmacotherapy for individual patients. But the truth is that precision medicine today is not tailored to individual patients; it is tailored to groups of patients. Precision drugs are tested on groups of patients that share a disease marker but other differences among patients are not taken into consideration. Once approved, the medicines produced on a bulk scale are prescribed to patients that share the disease marker specified on the drug's label. Built on the twentieth century drug development model, today's precision drugs still

Schellekens et al 2017

… but…

- Contentious and therefore secretive
- Under development (both the technical and the societal aspect)

Why is local production needed?

- Personalized drugs, precision medicine, rare diseases
- Smaller patient groups to recoup R&D investments: high prices

Possible solution: bedside production

- Bedside development, production and administration of off-patent biopharmaceutical product
- Distributed production has long history; known as magistral preparation, or compounding

TABEL I. Prijsvergelijking van enkele merkgeneesmiddelen en hun magistrale equivalenten

magistraal geneesmiddel volgens het FNA	*prijs per 10 g of ml*	*merkgenees-middel*	*prijs per 10 g of ml*
samengestelde triamcinolon-acetonide-oplossing	1,54	Kenalog-tinctuur	10,97
triamcinolonacetonidecrème 0,1%	1,43	Delphi-crème	1,34
hydrocortisoncrème 1%	0,53	Mildison-vetcrème	4,18
bacitracine-neomycinezalf	2,37	Nebacetin-zalf	4,98
clindamycine-oplossing 1%	11,60	Dalacin	13,09
tretinoïne-oplossing 0,05%	1,03	Acid A vit-lotion	3,31
fenylefrine-oogdruppels	0,11	Visadron	3,81
epinefrine-oogdruppels	3,31	Isopto-Epinal 1%	17,51
		Eppy	27,05
pilocarpine-oogdruppels 2%	7,04	Isopto Carpine 2%	7,79
lidocaïnezalf	1,35	Xylocaine	5,20

Scholten & Tel, 1991

How is bedside production done?

Make originator product by harvesting synthesized genetically engineered human or animal tissue to develop a cell line

Purification of cell line and in vitro modifications

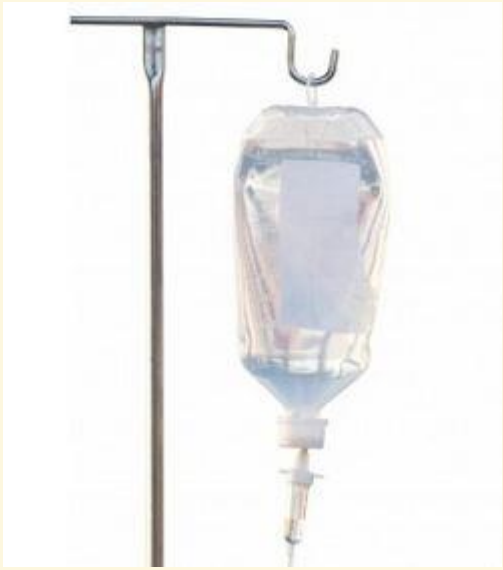
Shipped to academic hospital

Hospital pharmacist modifies/ personalizes product for individual patient

Contract research organization takes over rights of purified products

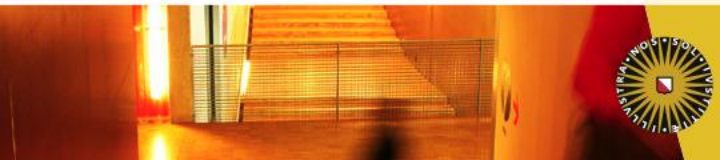
Administration to individual patient

Monitoring



Mixed-methods approach

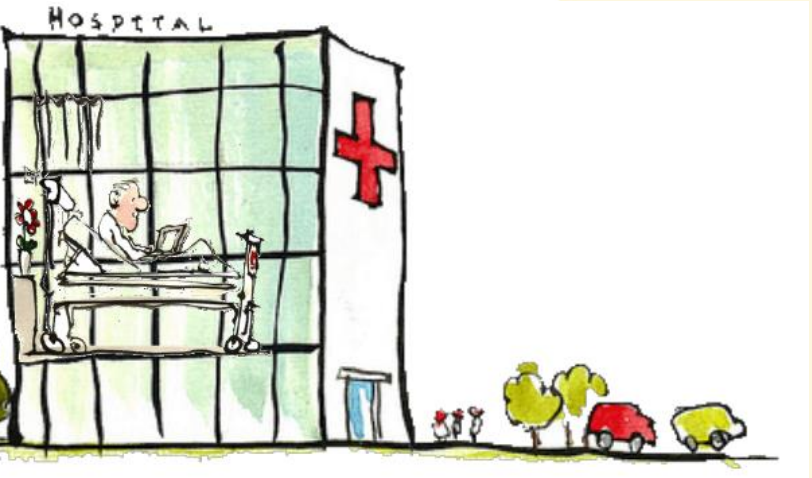
- Document analysis
- Interviews with e.g. hospital pharmacists
- Two focus groups (patients, medical specialists)
- Three dialogue workshops (including regulators, hospitals pharmacists, insurance companies, patients, doctors, etc.)



Why can hospitals do it?

Several regulatory possibilities/'loopholes':

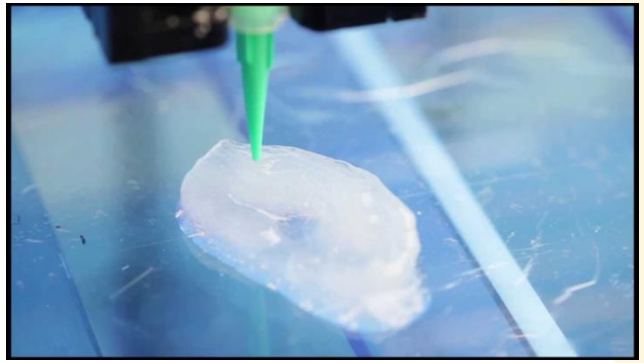
- Hospital exemption
  - "Producer gets permission to make Advanced Therapy Medicinal Products [gene therapy, stem cell therapy] despite these products not having a license […] for a specific patient […] in a specific hospital […] under exclusive professional supervision of medical specialist"



Why can hospitals do it?

Several regulatory possibilities/'loopholes':

- Home-brew innovation
  - No market exchange means no license needed
  - Major focus: Good Clinical Practice

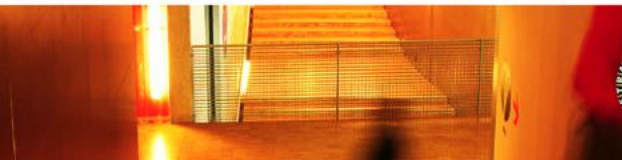


Why can hospitals do it?

- Not leaving hospital walls means no GLP regulation
- Dedicated tabletop production units (‘Bionespresso’)
  - For other medicines
  - For other application areas (warzones, remote areas etc.)
- Patient involvement?
- Storyline of magistral production

Identified issues

- Regulatory pressures: GCP (Health Inspectorate), European Medicines Agency
- Ethics evaluation board
- Reimbursement
- Pressures from IPR laws
- Medical guidelines and peer review
- Informed consent
- Risk governance; monitoring of safety and efficacy
- Public opinion, framing
- Litigation by incumbent firms



Part of wider development

- Other initiatives distributed manufacturing of drugs
- Similar to other emerging tech: 3D bioprinting, ATMPs, neglected diseases

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AMC zet farmaceut buitenspel met eigen medicijn

DO 5 APRIL, 12:13 AANGEPAST MA 9 APRIL, 09:35 BINNENLAND

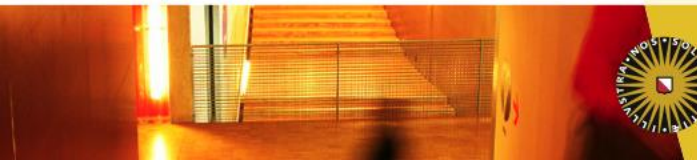
inspire 2 live

Apotheker gaat zelf medicijn tegen taaislijmziekte maken - tegen een fractie van de prijs

Paul Lebbink hoopt munitie te leveren aan discussie over hoge prijzen

Een Haagse apotheker hoopt binnen drie maanden het veelbesproken medicijn orkambi tegen taaislijmziekte na te kunnen maken tegen een fractie van de prijs die fabrikant Vertex rekent. De benodigde grondstoffen zijn al onderweg vanuit China, waar apotheker Paul Lebbink de spullen via internet heeft besteld.

Michiel van der Geest 21 november 2017, 22:59



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Linking issues with theories (1)

- Scalability: large-scale versus distributed, decentralised manufacturing:
  - New modular platforms in pharma
  - In designated manufacturing, smaller in size and cheaper to build and operate, dispensable
  - Potential of scalable production in remote areas and battlefields

Linking issues with theories (1)

- Strategic niche management:
  - 'local' experimentation versus global transfer
  - remain local, contextualized
  - protected spaces
  - distributed production vs. distributed consumption (see also Binz & Truffer, 2017) vs. distributed innovation

	Innovation		
Manufacturing		Global	Local
	Global		
	Local		

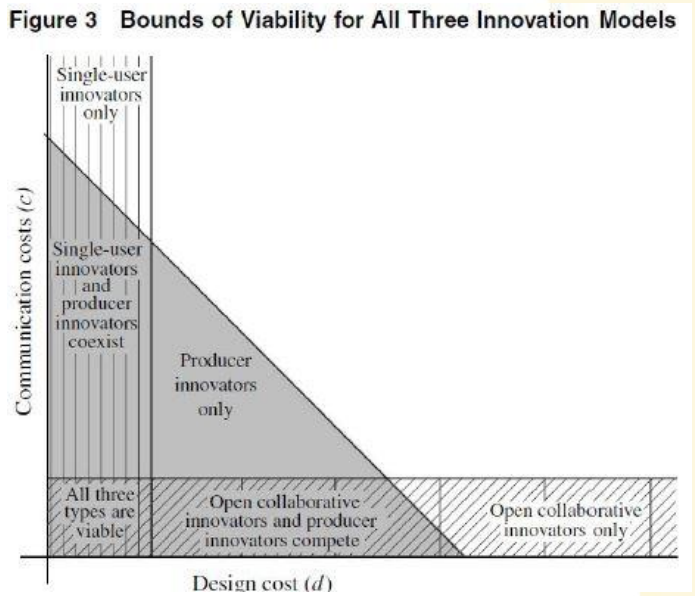
Linking issues with theories (2)

- Ensure sufficient levels of efficacy, safety and product quality

- Institutional entrepreneurs
  - Circumvent but also influence regulation
  - Through mobilizing allies, vision creation (relatedness)
  - Stretching boundaries of law
  - Aim: legitimization
  - Interesting role of patient organizations

Linking issues with theories (3)

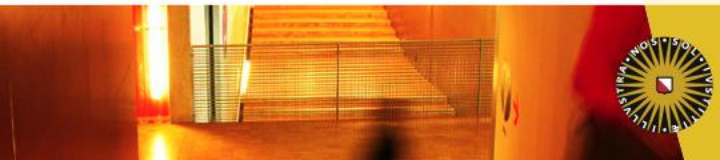
- Changing roles and responsibilities
  - of professionals (doctors, pharmacists becoming manufacturers)
  - drug developer and manufacturer
  - insurers as investors
  - Patients as safeguarders of quality
- User innovation?
- Toolkits for different contexts



Baldwin & Von Hippel, 2011

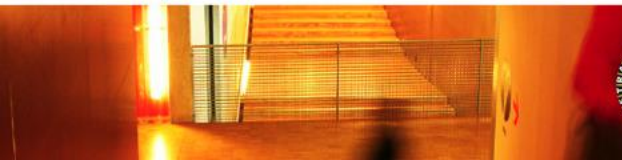
Smaller puzzle for innovation policy

- Need for link between autonomous bottom-up initiatives with structures in innovation (eco)systems:
  - Avoid capture in coordination
  - But also take e.g. incentives, IPR into account



Innovation policy instruments

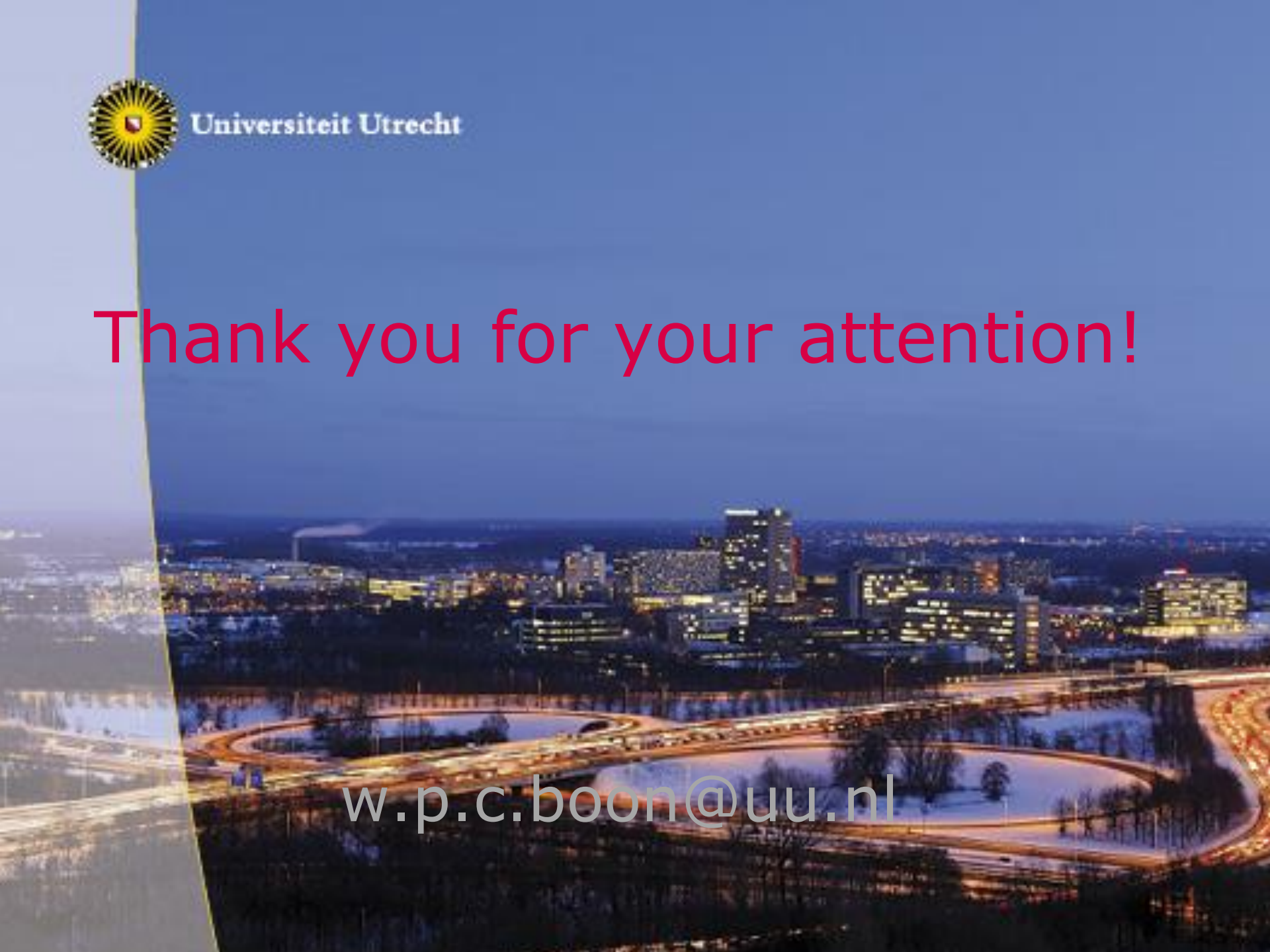
- Public-private partnerships
- Incentivize user innovation
- Experimentation in protective spaces/small-size, tentative innovation ecosystems



Bigger puzzle for innovation policy

- Address not only address market, system failures, but also transformational failures
- Move from mission (MDGs) to challenge orientation (SGDs):
  - more attention paid to implementation than to transfer
  - more attention to combine disciplines; sectors and challenges

Dye, 2018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