



How to stimulate innovation to reduce the environmental cycle of medicines and multi-resistant bacteria

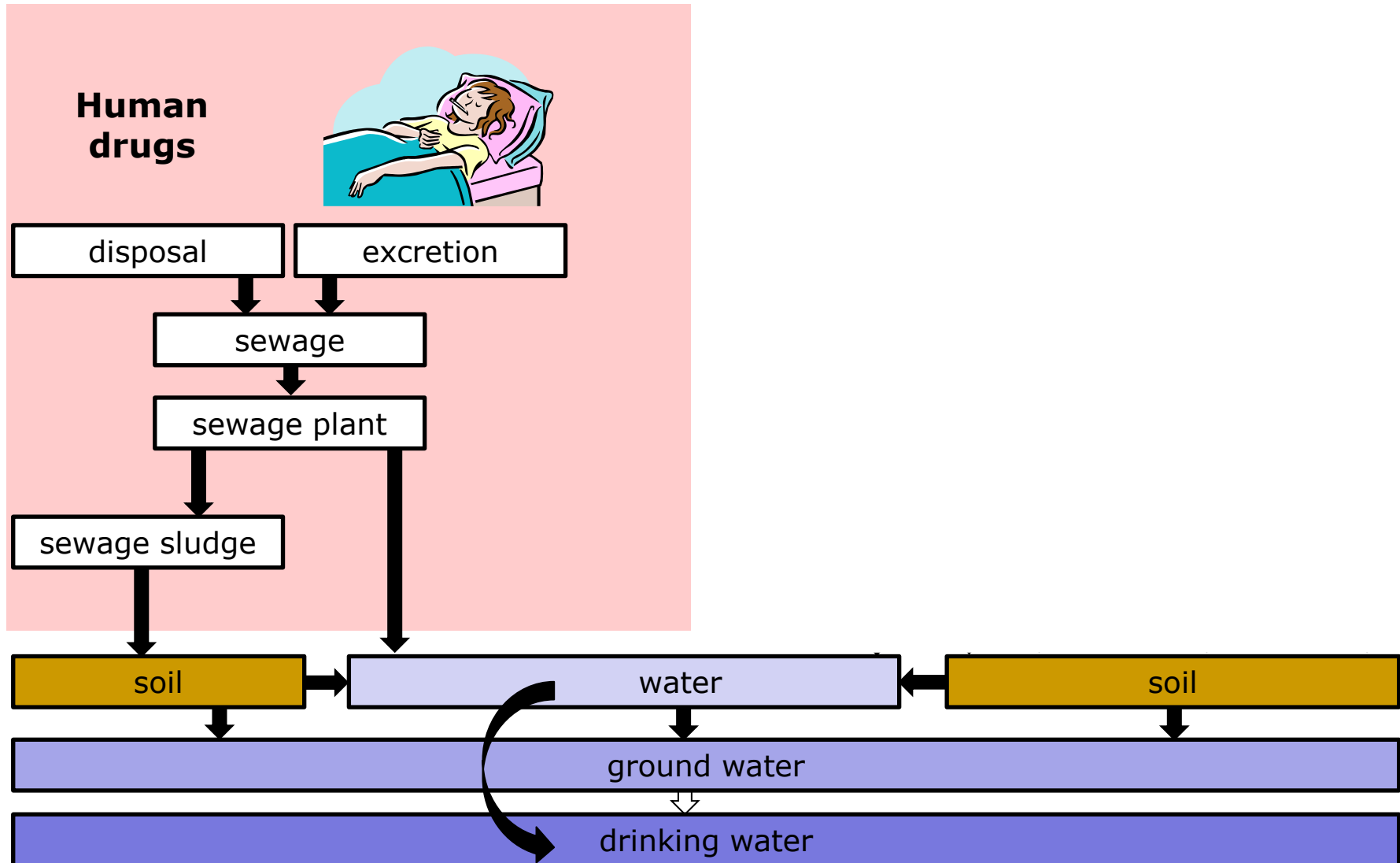
Dr. Maximilian Hempel
Deutsche Bundesstiftung Umwelt

CONTENT

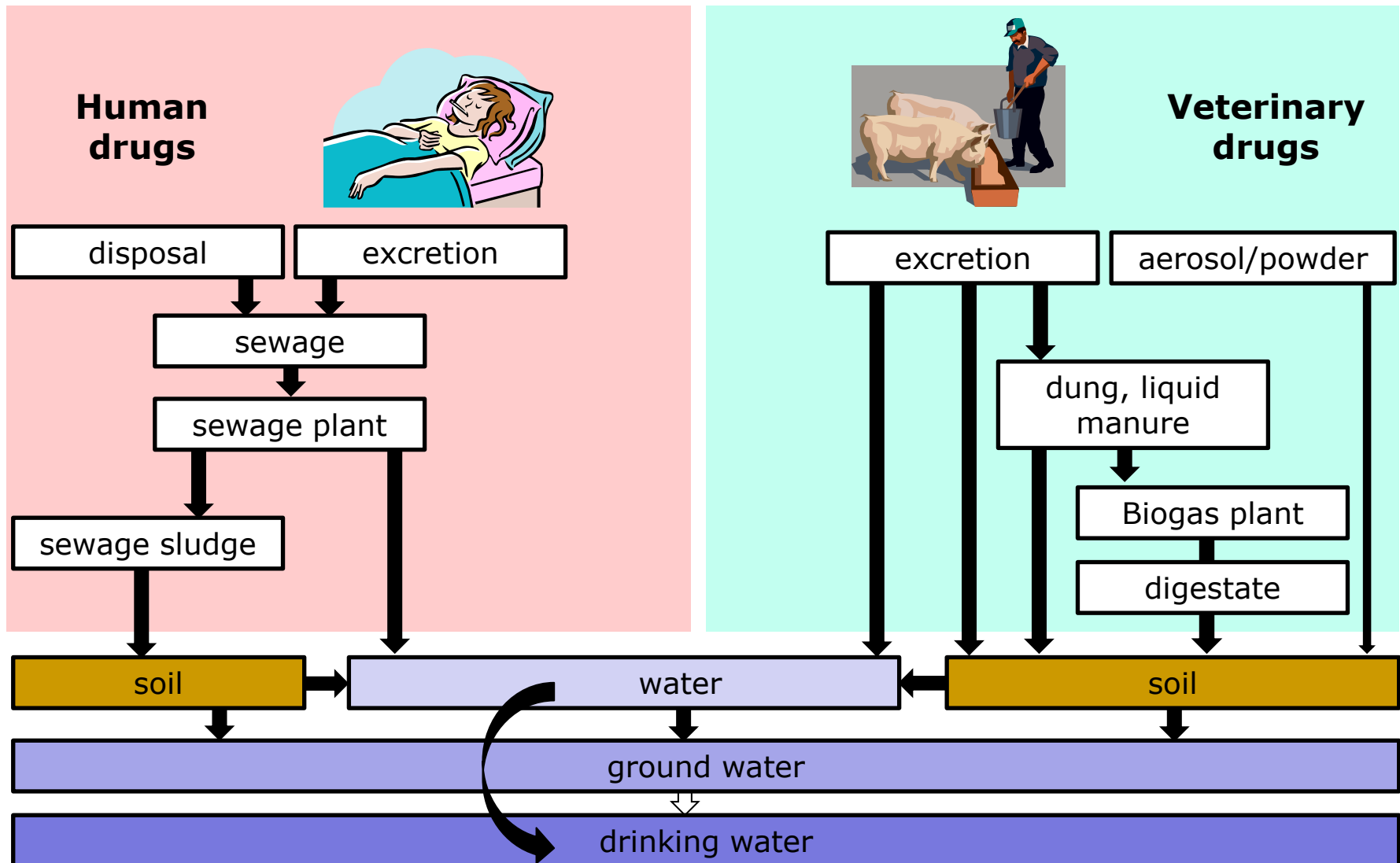


- 1. DBU initiative „Sustainable Pharmacy“ and some project examples**
- 2. How to apply for funding at DBU**

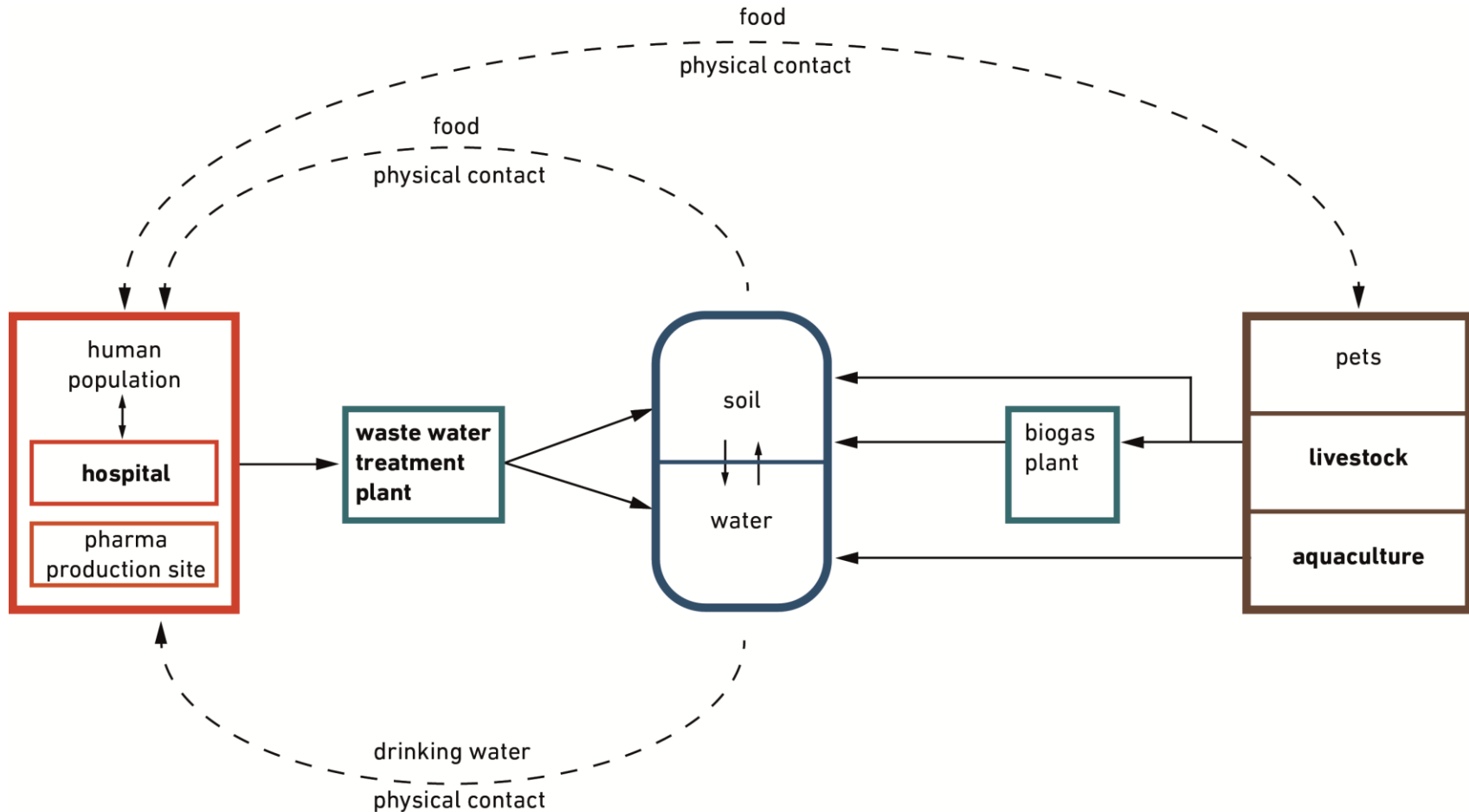
Emission pathways of pharmaceuticals entering the environment



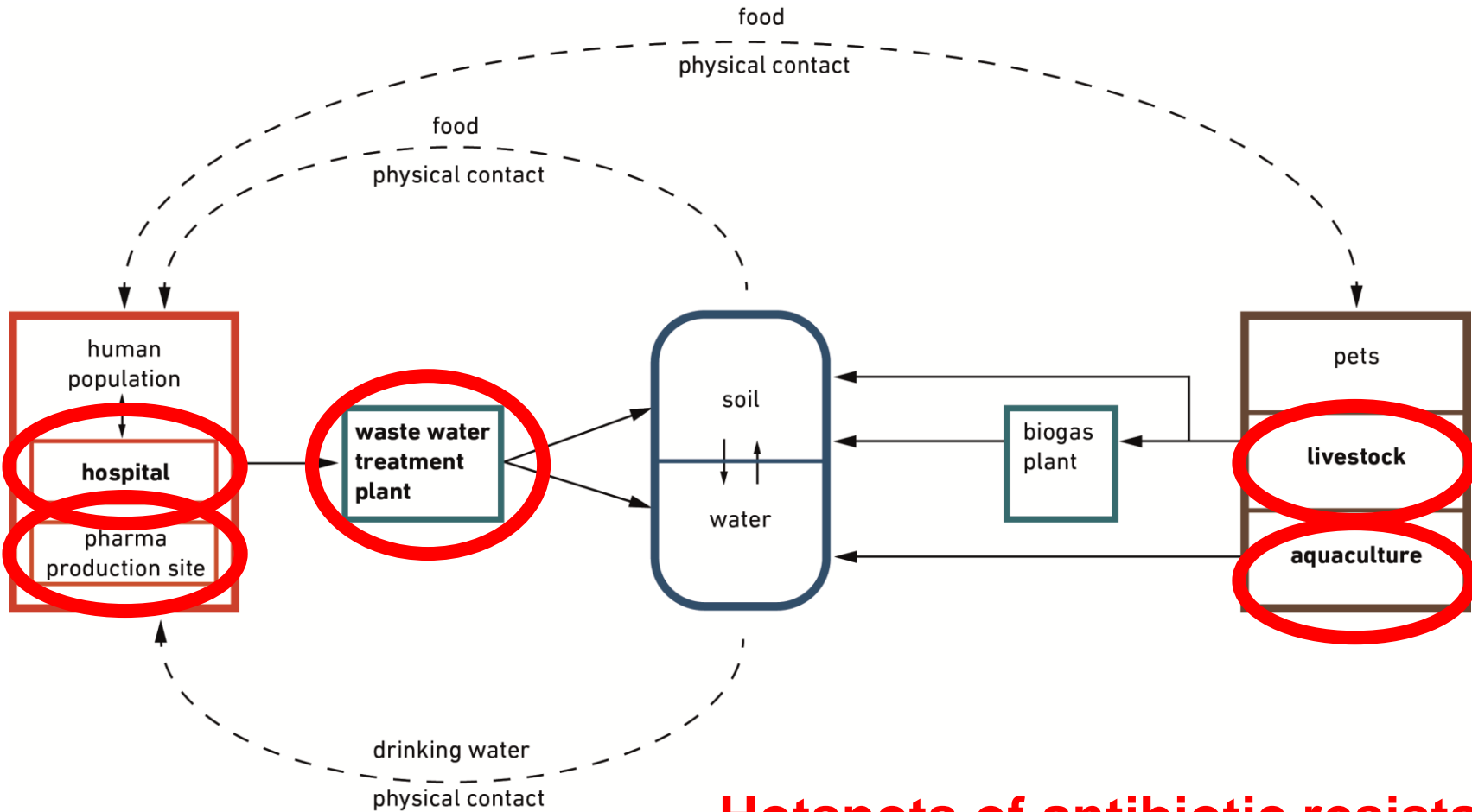
Emission pathways of pharmaceuticals entering the environment



Dissimination of antibacterial agents and antibiotic resistances in the environment



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Hotspots of antibiotic resistances

Approaches for a more sustainable pharmacy



European authorization of pharmaceuticals:

- environmental risk assessment of veterinary (since 1998) and human (since 2006) pharmaceuticals
- Restrictions, if environmental risks are proven

Approaches for a more sustainable pharmacy

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But...

- only relevant for **new** drugs
- environmental risks not relevant for approval of **human** pharmaceuticals
- No subsequent assessment of older drugs
- Example for denied approval: contraceptive for pigeons
 - Efficacy unclear, ecological effects and chemical fate of active ingredients ethinylestradiol und levonorgestrel



SHORT-, MEDIUM- AND LONG-TERM MEASURES FOR REDUCTION OF PHARMAECUTICALS IN THE ENVIRONMENT

Table 1

Short-, medium- and long-term measures for the reduction of pharmaceuticals in the environment.

Precedence	Human Pharmaceuticals	Veterinary Pharmaceuticals
Short-term	<ul style="list-style-type: none"> • Avoid questionable prescriptions • Regular education and training of doctors and medical staff • Improvement of hygienic standards and hospital management • Avoid the disposal of pharmaceuticals via sink or toilet • Implementation of a take-back system for drugs • Development of technical processes to eliminate trace substances in sewage treatment plants • Reduce effluent emissions from pharmaceutical production facilities • Extensive monitoring of active ingredients in the environment and their impact on living organisms 	<ul style="list-style-type: none"> • Avoid questionable treatment • Improvement of hygienic standards and stable management • Improvement of animal health and well-being by, e.g., special feeding and prophylactic vaccination • Use of microbial degradation of vet pharmaceuticals in manure by passive storage or anaerobic fermentation in biogas plants • Extensive monitoring of active ingredients in the environment and their impact on living organisms
Medium-term	<ul style="list-style-type: none"> • Change prescriptions to more environmentally-friendly drugs • Change galenics of drugs to minimize the excretion of the active ingredients • Inclusion of relevant aspects of pharmaceuticals for the environment to sustainability and environmental reports of pharmaceutical enterprises 	<ul style="list-style-type: none"> • Changes in formulation and application of drugs • Change of dosage and galenics of drugs to minimize the excretion of active ingredients • Development and implementation of dosage systems for drugs in stables
Long-term	<p>Human and veterinary pharmaceuticals</p> <ul style="list-style-type: none"> • New development or redesign of pharmaceuticals, e.g., addressing "benign by design" or drug targeting • Improvement of diagnostics to personalize healthcare, e.g., personalized medicine • Incentives for pharmaceutical manufacturers to design benign products 	

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DBU - initiative „sustainable pharmacy“



Goals:

- Reduce the emission and the impact of pharmaceutical residues in the environment
- increase resource-efficiency production of pharmaceuticals
- 3 calls (20.8.2012, 5.11.2013, 15.1.2015)
- Funded projects:

year	Funded projects (applied projects)	Subsidies (Total costs of the project)
2013	6 (31)	2,5 Mio. € (4,0 Mio. €)
2014	7 (31)	2,6 Mio. € (3,8 Mio. €)
2015	5 (23)	1,9 Mio. € (2,8 Mio. €)
2016	1	0,4 Mio. € (0,4 Mio. €)
total	19	7,4 Mio. € (11 Mio. €)

Can biogas plant eliminate antibiotics?



Issue:

200 Mio. t manure contain ca. 200 t antibiotics (Germany 2014)

Project goals:

- Increase eliminating rate for antibiotics
- Investigate fermentation process by varying the process parameter and adding enzymes
- Develop recommendations for biogas plants



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results:

- A slight reduction of emitted sulfonamides and tetracyclines
- But: antibiotics are not eliminated, but adsorptive bound to substrate
- **Biogas plants are no barrier for antibiotics !!!**



Is sow cycle control possible without drugs with endocrine function in the environment ?



Situation

- In pork farming ovulation is synchronized by medicinal cycle control
- Advantageous for feeding, hygienic status & livestock health
- But: endocrine function of drugs

Goals:

- Develop a time-released drug using a peptide hormone
- agent (Gonadorelin[6-D-Phe]) is completely metabolized in the animal



Veyx-Pharma GmbH , Universität
Leipzig , LMU München, L.B. Bohle
GmbH,
subsidies: 1.055 T €; 2013 – 2019
DBU AZ 30815-32 & DBU AZ 33529-32;

Current status:

- waiting for results of pre-clinic and endocrinological results

Can mastitis be treated without antibiotics?

Goals:

- Develop a therapeutic agent with living lactic acid bacteria
- Reduce the use of antibiotics and prevent the formation of antibiotic resistance
- Reduce the loss of milk due to waiting times

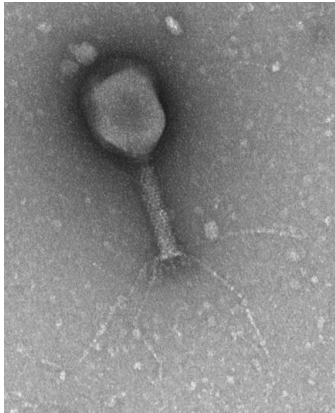


Results:

- bacteria are effective for mastitis treatment
- Bacteria are cultivatable, stable, storable
- Next: application concept and field studies



Can Bacteriophages help to reduce the amount of antibiotics in poultry husbandry ?



Situation

- Large amounts of antibiotics used in poultry husbandry
- high rates of antibiotic resistance, e. g. ESBL-E. coli

Goals:

- Use bacteriophages, the natural antagonists of bacteria, to reduce resistant germs specifically
- Reduce amount of antibiotics by 30%

Current status:

- Ongoing project; laboratory and stable experiment produce different results; time of dosage seems to be important;

Can galenic formulation help to minimize emission of pharmaceuticals?

Project goals:

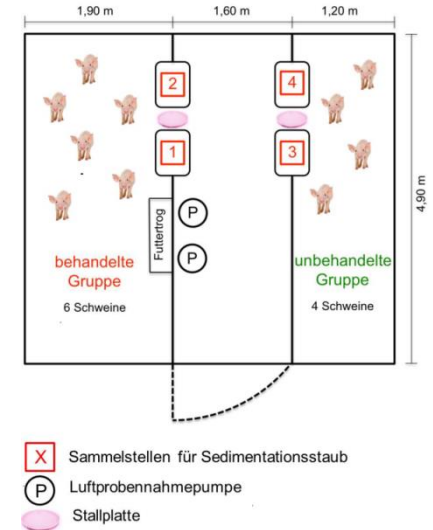
- Improved formulation for oral medication
- Reduce contamination in the stable's surrounding
- Prevent residues of pharmaceuticals in drinking troughs

action plan:

- improve the bioavailability of drugs to reduce the amount of the active substance → less excretion
- develop physical methods in order to reduce drug residues in water pipelines

Current status:

- Ongoing project; optimized formulation produced; in-vivo-experiments with pigs in a stable are running



Is it possible to develop degradable Pharmaceuticals?



Problem:

- Cyprofloxacin is a widely used antibiotic
- Cyprofloxacin frequently detected in water samples

Goal:

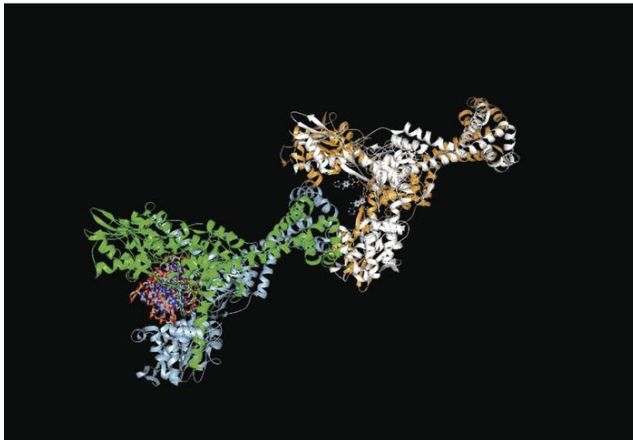
- Benign alternative for Cyprofloxacin
- Degradable after leaving the body

Procedure:

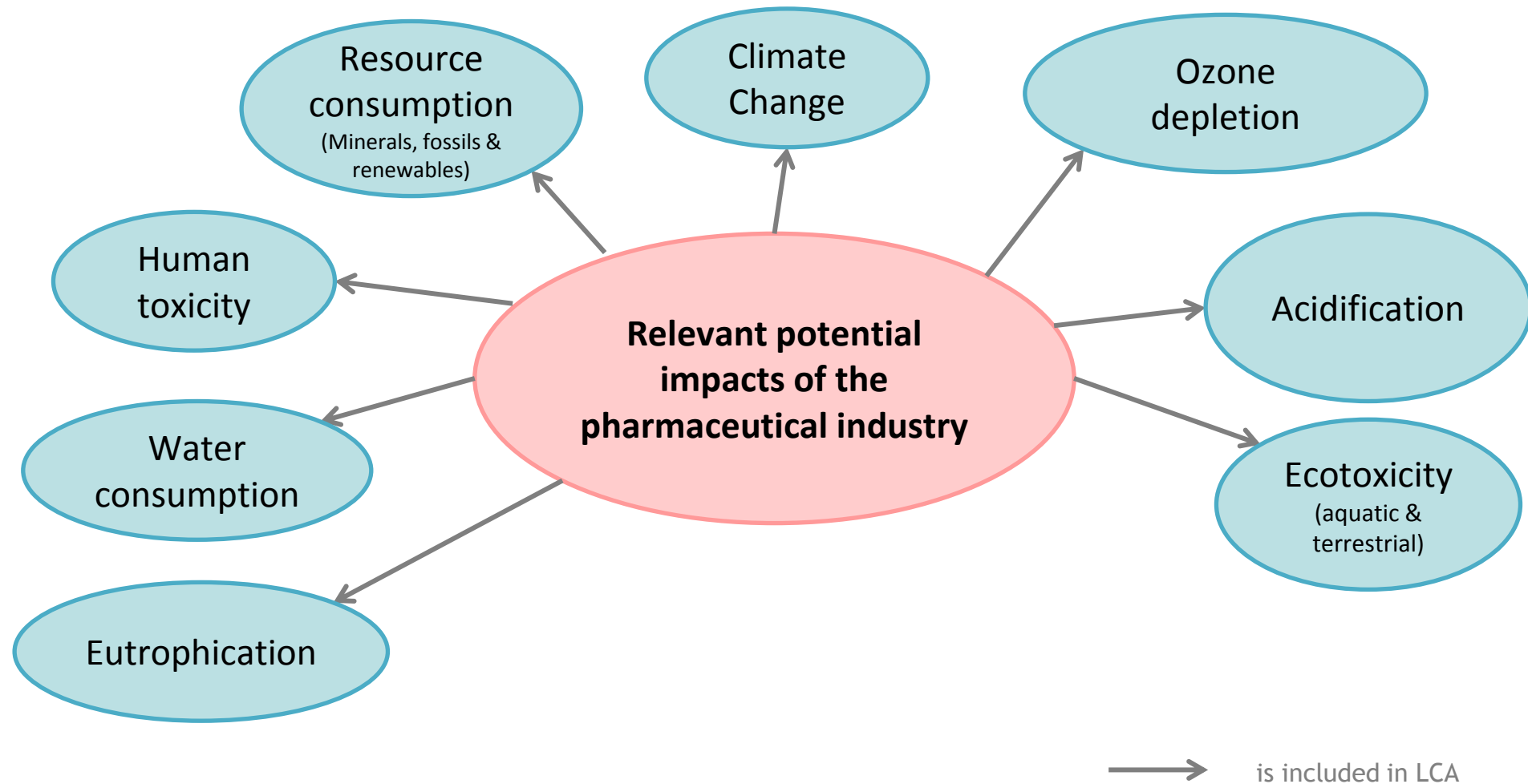
- Using QSAR (Quantitative Structure-activity relationship) for prediction

Results:

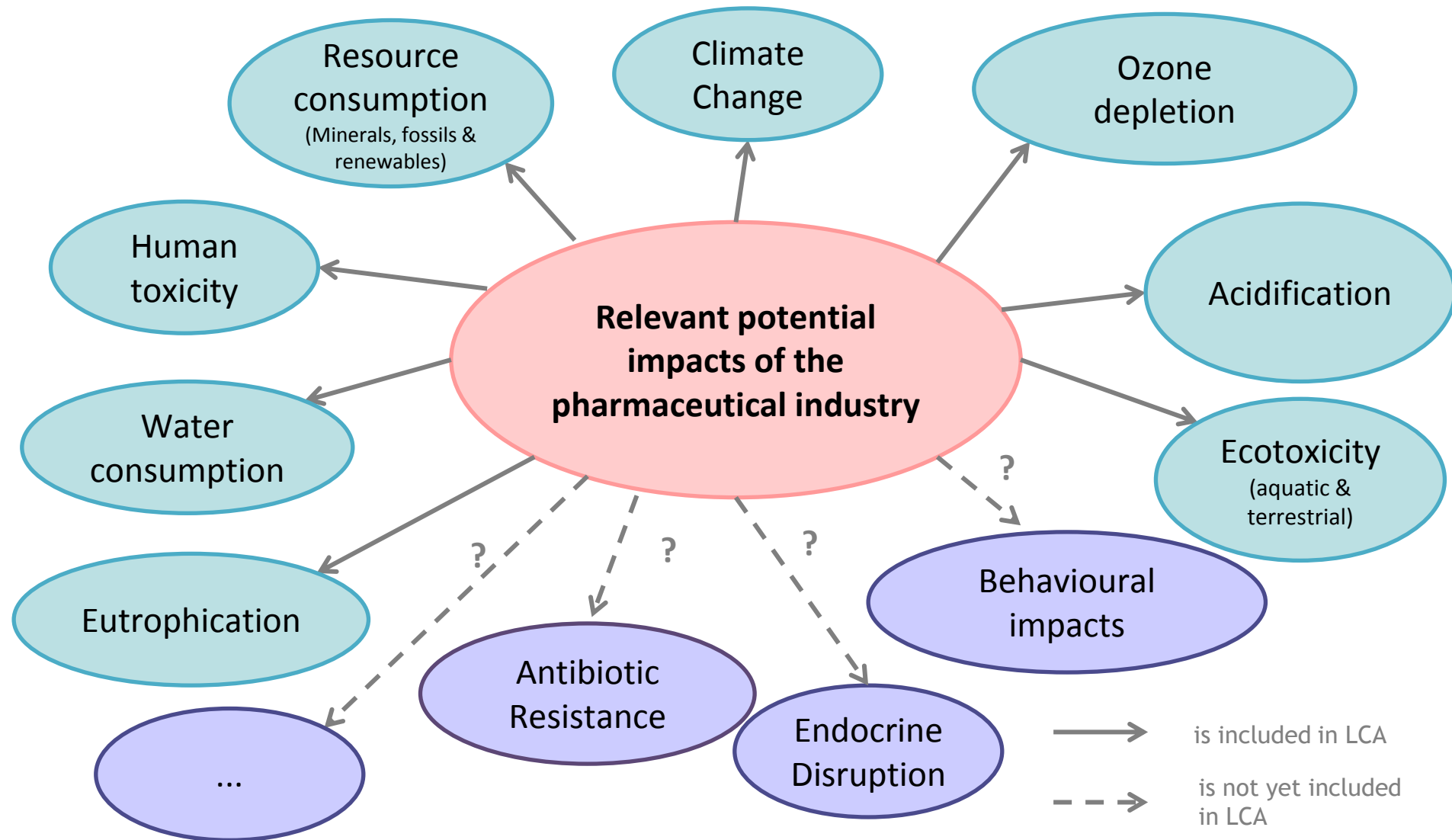
- Improved new lead compound
- Synthesis of new antibiotics; degradation test afterwards = successful
- **BUT:** Till now no industrial partner



Is the actual sustainability assessment in the pharmaceutical industry appropriate?



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Deutsche Bundesstiftung Umwelt

- founded in 1990
- 1.28 bn € endowment capital, today 2,2 bn €
- appr. 50 mio € for project funding p. a.



criteria

- innovation
- exemplary
- environmental benefit

A typical project, funded by DBU

- Small/medium enterprise is engaged
- Cooperation of partners (can, does not have to)
- Typical finance volume: 100 - 400 T€
- Duration: 12 – 36 months
- Financing of enterprises: 50%
 - salary, overhead, material costs, travel expenses, contracts
- Financing Universities: 100 %
 - salary, material costs, travel expenses, contracts (no overhead)

What to do?

Find a German partner (university, enterprise, NGO, ...)

Write a short proposal (3-6 pages, German) ← - - - - -

DBU is evaluating

Who is applying?

What is the aim of the project?

Costs? Duration time?

Revise and
adopt

Write a complete proposal (workplan, costs, ..) ← - - - - -

DBU & extern experts are evaluating

decision

Revise and
adopt

THANK YOU FOR YOUR ATTENTION

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