Benign by Design:
Rethinking Pharmaceuticals from the Molecule Up

Prof. Dr. Dr. h. c. Dr. h. c Klaus Kümmerer

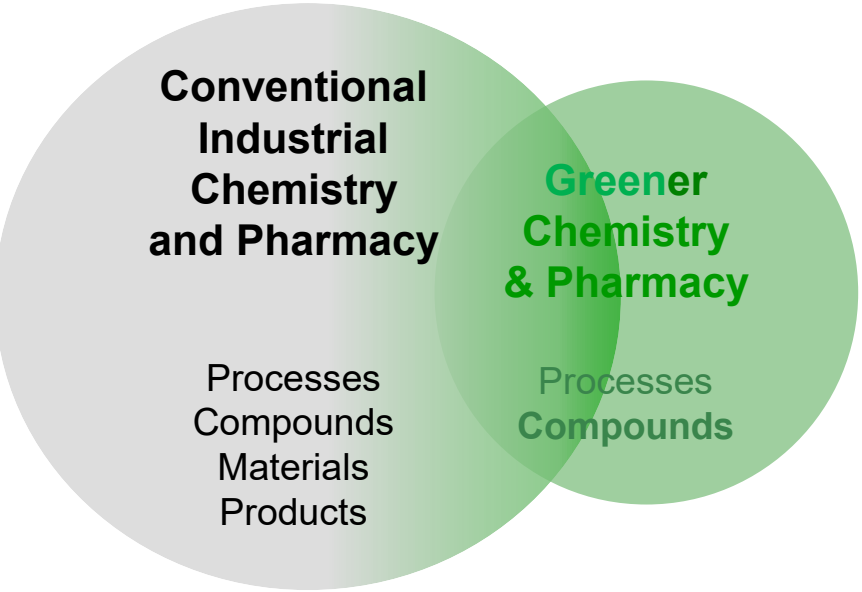
Professor of Sustainable Chemistry and Material Resources

Content of this Lecture

- The bigger Picture Green Pharmacy vs. Sustainable Pharmacy
- A Corner Stone: Benign by Design
  - Why needed
  - How to do
  - Examples

Greener Is Not Necessarily More Sustainable!

K. Kümmerer, Angewandte Chemie International Edition (2026): e3329101. https://doi.org/10.1002/anie.3329101



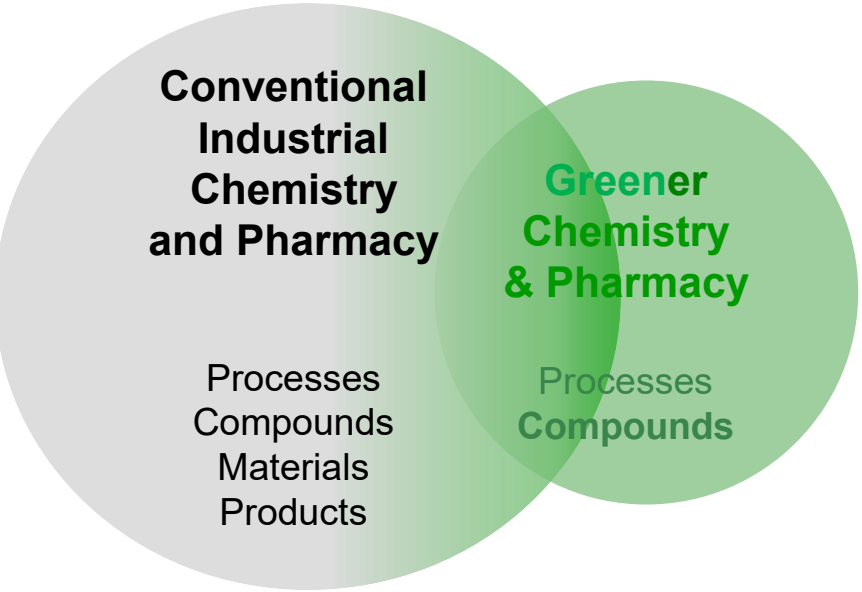
Basis of Sustainability:

- Sufficiency
- Consistency
- Efficiency
- Environment
- Economy
- Social
- Systems Thinking

Non sustainable **Greener** **Increasingly sustainable**

Greener Pharmacy -> Greener Chemistry -> Pollution Prevention

K. Kümmerer, Angewandte Chemie International Edition (2026): e3329101. https://doi.org/10.1002/anie.3329101



Non sustainable **Greener**

Pollution Prevention already commercialised in industry in 1970s and 1980s

United Nations. Non-Waste Technology and Production. A Seminar of the United Nations Economic Commission for Europe (Pergamon 1978).
Royston, M. G. Pollution Prevention Pays. (Pergamon 1979).
Sheldon, R.A. E-Factor Chem. Ind. 903–906 (1992)
Tundo, P., Aricó, F. Chem. Int. 29, 4-7 (2007)
Murphy, M.A. Early industrial roots of green chemistry “Pollution prevention efforts during the 1970s and 1980s. Chem. Int. January-March, 21-25 (2021)
Krasnodębski, M., 2022. Lost Green Chemistries: History of Forgotten Environmental Trajectories', Centaurus, 64, 509–536

Term „Green Chemistry“ invented in Italy 1987

Pasquon, I., Zanderighi L., 1987. La Chimica Verde. Milano, Hoepli.
Promoted only by U.S. EPA early 1990s

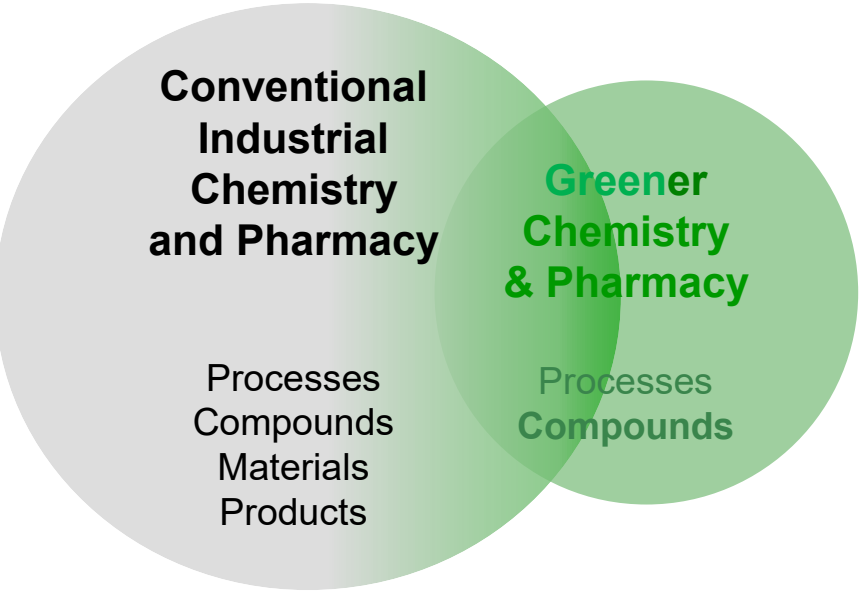
1989 First industrial project on biodegradable polymers (Italy)

EC Council Directive 96/61/EC 1996 - integrated pollution prevention (legislation, not just chemical industry), law

„Summary“ in 1998, 12 Principles of Green Chemistry (Anastas & Warner), **voluntarily only**

The Realm of Greener Chemistry

K. Kümmerer, Angewandte Chemie International Edition (2026): e3329101. https://doi.org/10.1002/anie.3329101



Focus on Synthesis and some properties of individual chemicals

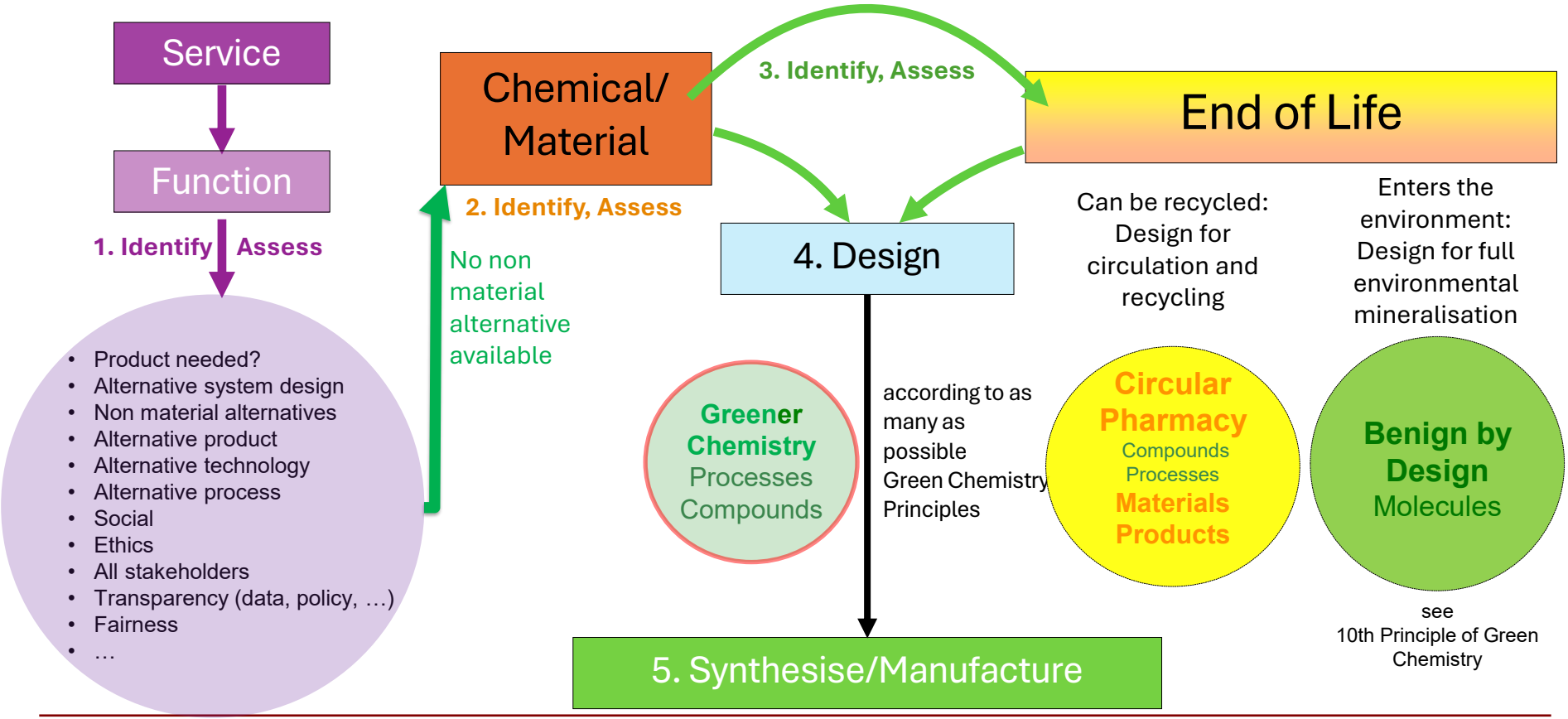
- **Less Waste**
- **Less Energy**
- **Less Hazardous**
- **Renewable resources**

10th Principle of Green Chemistry: Design for Degradation

Non sustainable → **Greener**

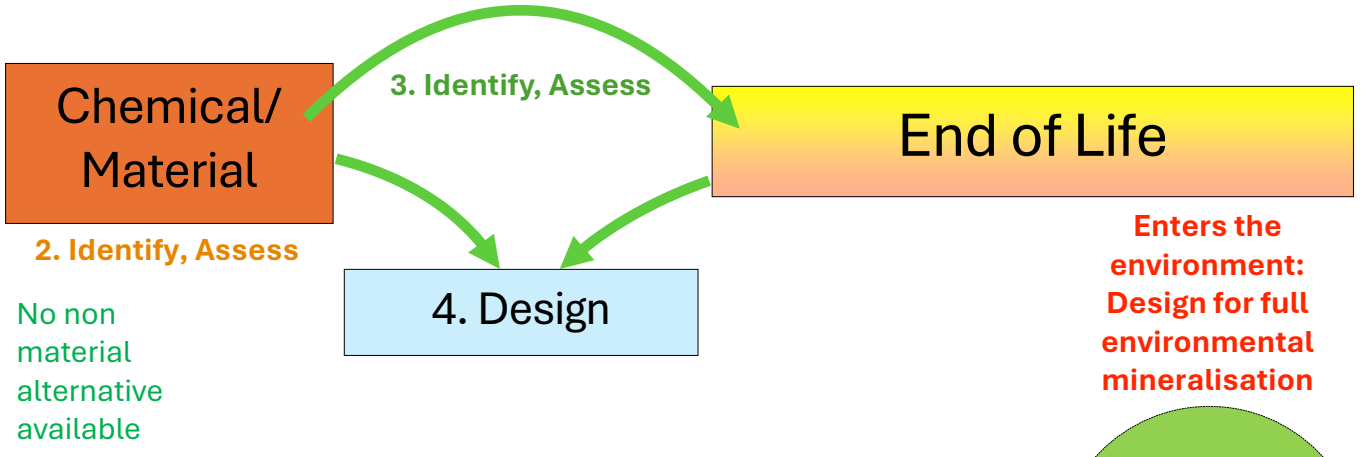
More Sustainable and Greener Pharmacy - Workflow

K. Kümmerer, Angewandte Chemie International Edition (2026): e3329101. https://doi.org/10.1002/anie.3329101



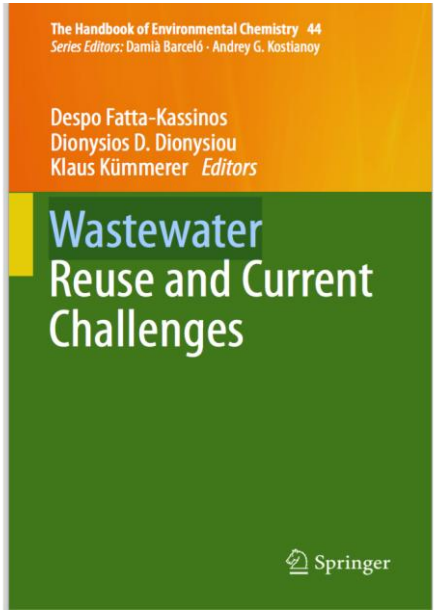
Benign by Design - Workflow

K. Kümmerer, Angewandte Chemie International Edition (2026): e3329101. https://doi.org/10.1002/anie.3329101

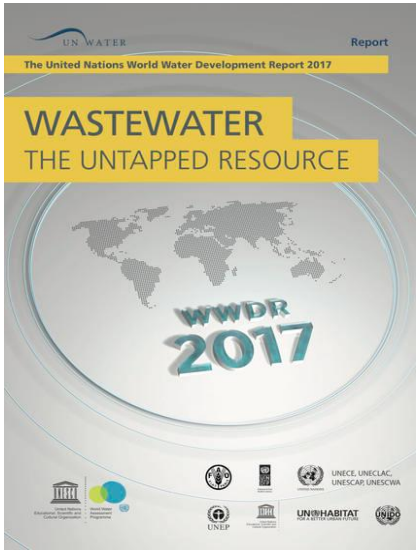


Drivers for Benign by design-Water Needs

Increasing Need for Water Reuse exacerbated by climate change

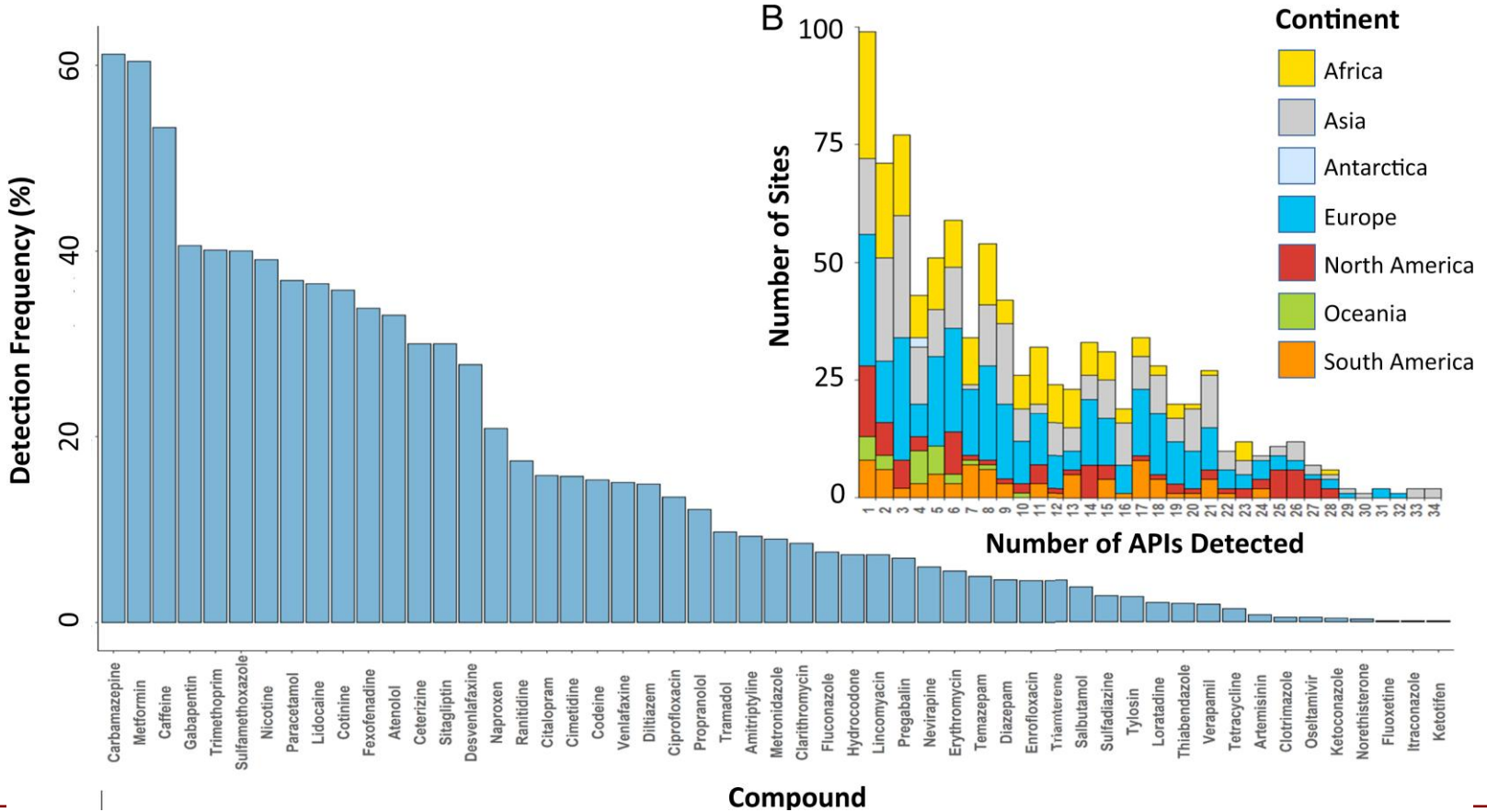


> 80% of Waste Water not treated (globally)

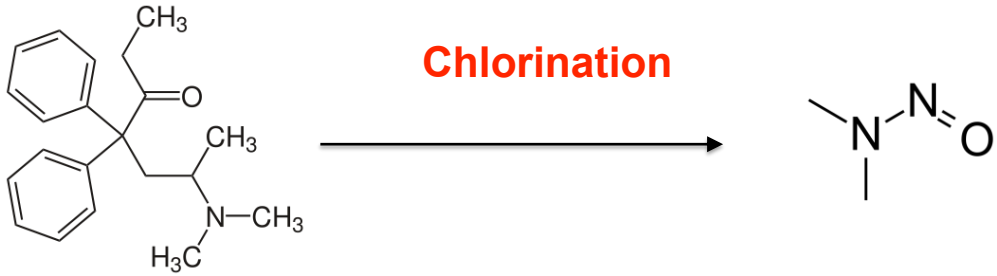


Pharmaceuticals in Rivers Worldwide

Wilkinson, J.L. et al. Proc Natl Acad Sci., 2022;119:e2113947119



Highly Toxic Transformation Product of Advanced Effluent Treatment and Drinking Water Disinfection



Methadone

Hanigan et al., ES&T, 2015

N-Nitrosodimethylamine (NDMA)

- Highly hepatoxic
- Suspected human carcinogen
- **Threshold U.S. drinking water: 7 ng/L**

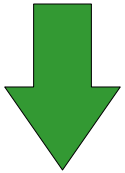
Other precursors: pharmaceuticals, pesticides, DOC, ultra filtration membranes, …
(e.g. Ersan et al. ES&T Lett. 2, 66-69 Marti et al., Water Research 72, 262–270)

Environmental Persistence of pharmaceuticals, their metabolites and transformation products

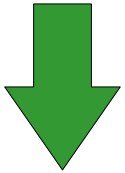
Kümmerer K. (2007), Green Chemistry, 9, 899–907

Active Pharmaceutical Ingredients, Adjuvants, Excipients

Ready and full (bio)mineralisation in the environment



No exposure



No effects, no risk!

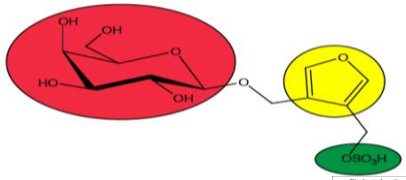
Biodegradability in the Aquatic Environment (in %) - **Without** Being Designed for it!

API	OECD 301 D	OECD 301 F	OECD 302 B
Valproic acid	72	78	
Mesalazin	> 90	> 90	
Acetylsalicylic acid		81	
Penicillin V			> 90
Piperacillin	20		
Amoxicilin	80		
Hydroxamic acid	50	90	
Piracetam		> 90	> 90

Längin A., Aley R., König K., Kümmerer K. (2009) Chemosphere 75, 347–354; unpublished

Benign by Design for Pharmaceuticals

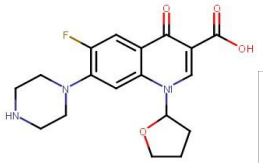
Anti Cancer API



EP 2 474 552 A1
(DKFZ Heidelberg)

Kümmerer K (2019): Sustainable Chemistry and Pharmacy, 12 (2019) 100136

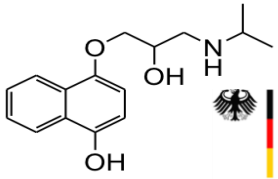
Antibiotics



WO2019072905A1
WO2019072907A1

Leder C, Suk M, Lorenz S., Rastogi T, Peifer C, Kietzmann M, Jonas D, Buck M, Kümmerer K (2021) ACS Sustainable Chem. Eng. 9, 28, 9358–9368

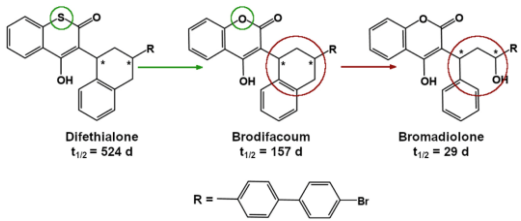
ß- Blockers



Bundesministerium für Bildung und Forschung

Rastogi T, Leder C, Kümmerer K (2014) Env. Sci Technol. 111, 493–499 (**Propranolol**)
Rastogi T, Leder C, Kümmerer K (2014) Chemosphere 111, 493–499 (**Metoprolol**)
Rastogi T, Leder C, Kümmerer K (2015) RSC Adv. 5, 37, 29124–29134 (**Atenolol**)

Rodenticide



Hohenberger J, Friesen A, Wieck S (2022) Sustainable Chemistry and Pharmacy 25, 100602

Umwelt Bundesamt

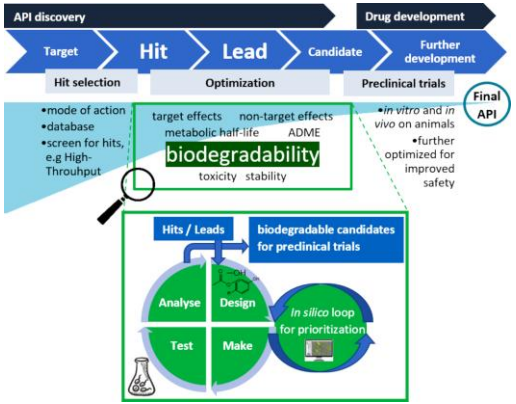
Excipients Selection Guide

Bading,M, Griffing M., Olsson O, Harris J, Scher J, Sakurai A, Overcash M, Kümmerer K (2025) Green Chemistry, 27, 15568–15581

Boehringer Ingelheim

Benign by Design for Pharmaceuticals

Integration into the industrial drug design process



Puhlmann N., Mols R, Slotweg C, Kümmerer K. (2021), Green Chem, 23, 5006-5023

Moermond CTA, Puhlmann N, Brown AR, Owen SF, Ryan J, Snape J, Venhuis BJ, Kümmerer K (2022), Environ. Sci. Technol. Lett., 9, 699-705

Vidaure et al., Design of greener drugs: aligning parameters in pharmaceutical R&D and drivers for environmental impact. Drug Discovery Today, 29, (7), July 2024

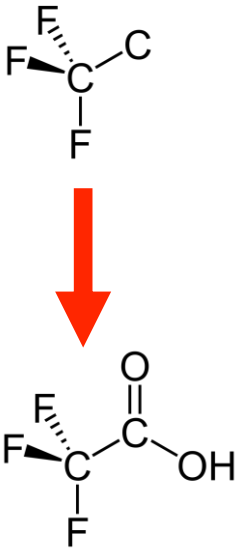
PREMIER
PRIORITISATION AND RISK EVALUATION OF MEDICINES IN THE ENVIRONMENT

Develop exting Design rules further

e.g. Assessment of Role of F

Highly Toxic and Persistent Transformation Product: Trifluoracetic Acid (TFA)

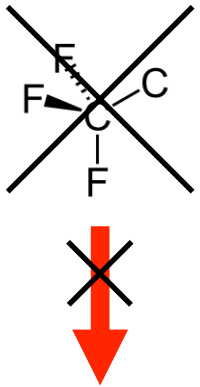
- Environmental degradation product of organic chemicals and pharmaceuticals containing



- Highly mobile, highly prescient (PMT, vMvP)
- Highly toxic (e.g. reproductive toxicity 1B)
- Ubiquitous (air, water, soil, food, organisms)

PFAS Moiety is often not Needed

- C-CF3 moiety most often not needed



can be avoided -> no TFA

Greinke J, Mußler P, Maack G, Hug M J, Müller, M Speichert G: Per- and polyfluorinated active pharmaceutical ingredients: Overview and alternatives. Sustainable Chemistry and Pharmacy, 52, 102416 (2026)

Incentives

- Need for clean water
- Upcoming legislation
- Corporate Sustainability
- Green consumer (patient)

- Future?
  - Prolonged patent life time
  - Fast Track authorization
  - New patentable compounds

Benign by Design – Summary

Efficacy

+

Environmental (Bio)degradability

<u>Not in Opposition !</u>

Fast and full environmental degradation:

- **No exposure**
- **No effect**
- **No risk !**

Opportunities for innovation and new compounds.

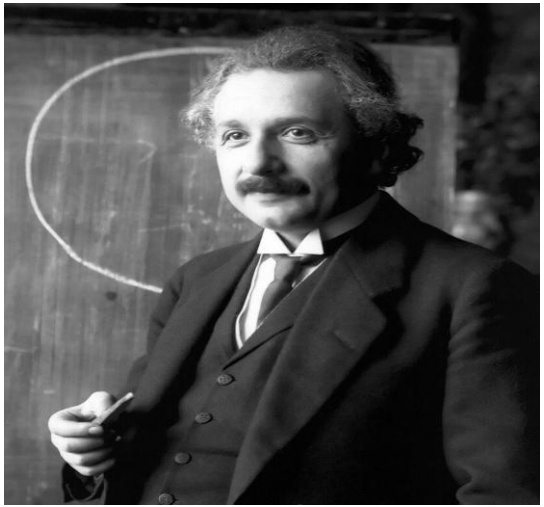
New Businesses Opportunities

More success stories needed

Full life cycle view necessary

A smart person solves a problem.

A wise person avoids it.



Attributed to Albert Einstein