

Benign by Design: Rethinking Pharmaceuticals from the Molecule Up

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Professor of Sustainable Chemistry and Material Resources



EDC

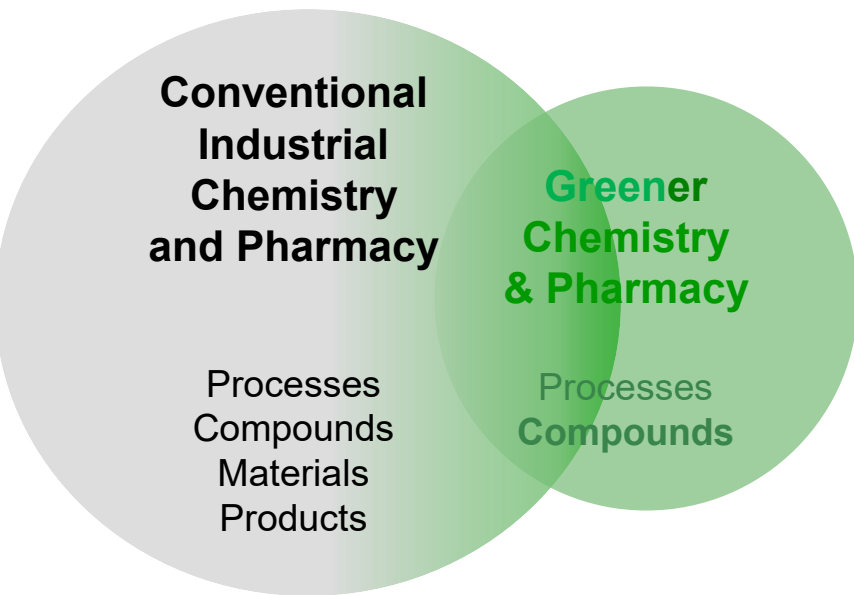
EVALUATION AND
DESIGN OF CHEMICALS



- 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>



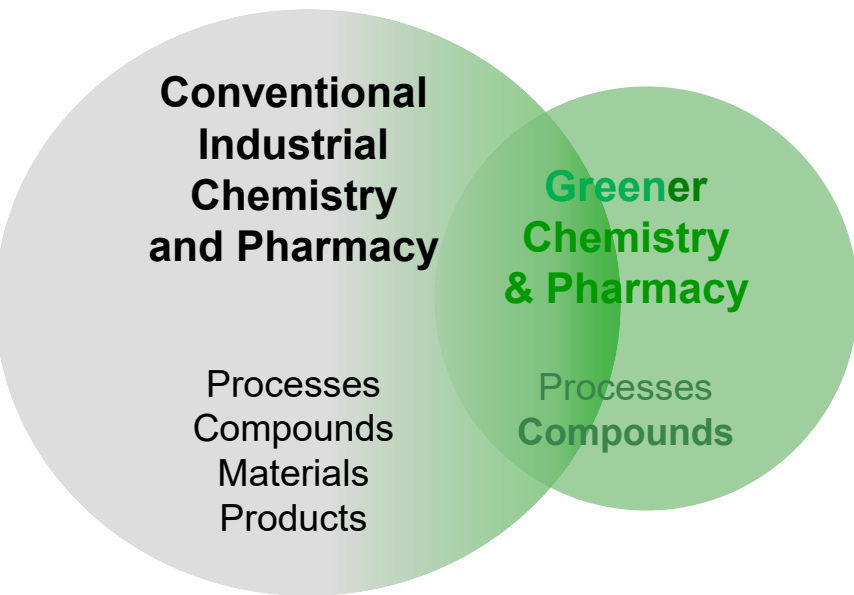
Basis of Sustainability:

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



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

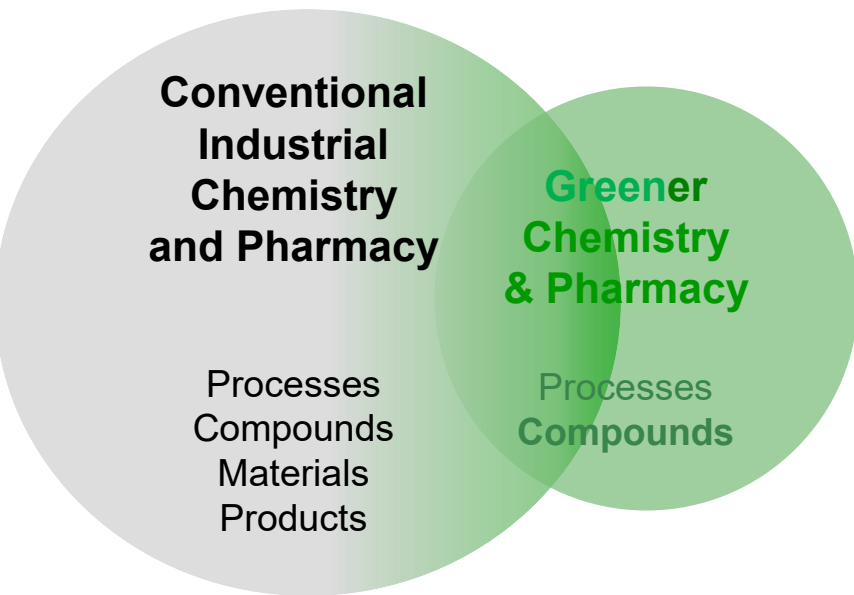
1989 First industrial project on biodegradable polymers (Italy)

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**

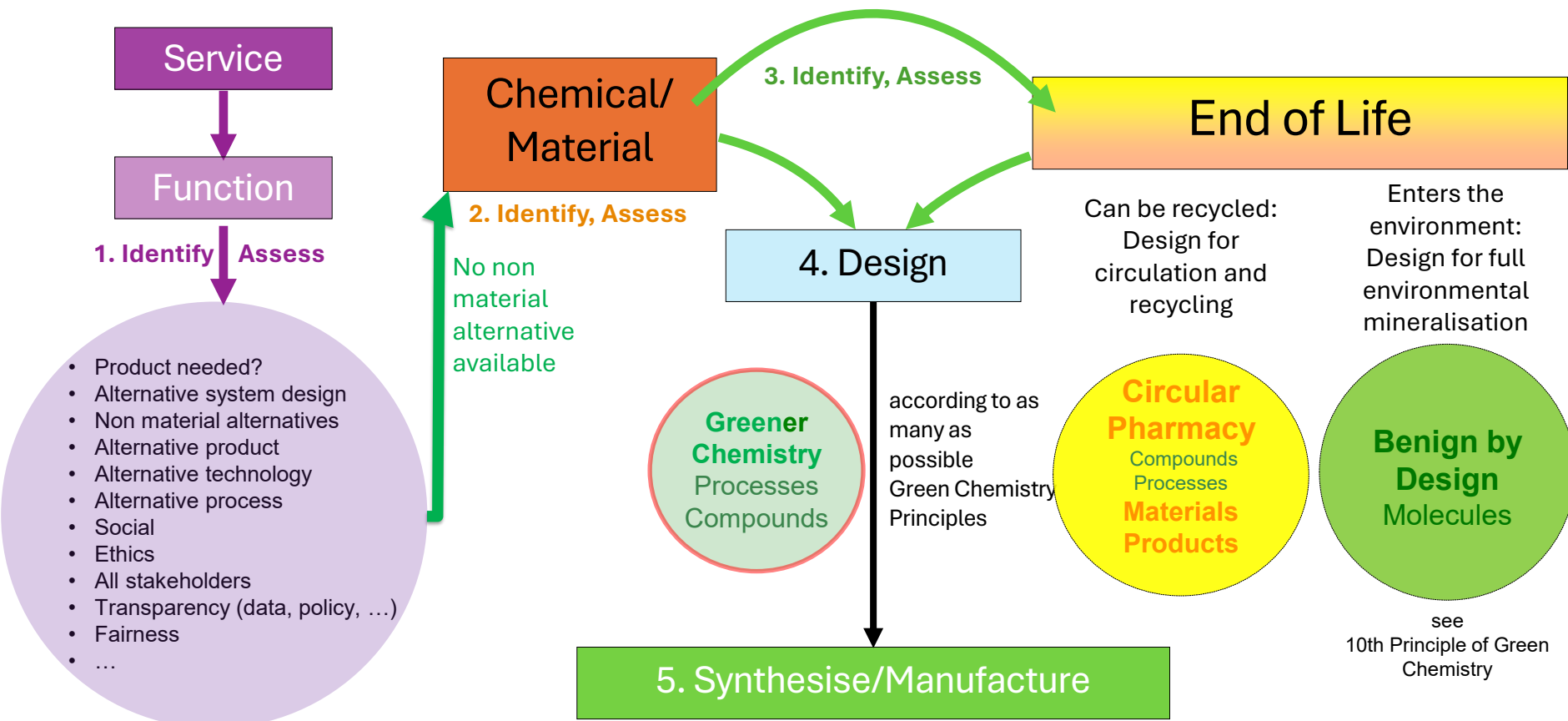
Non sustainable

Greener



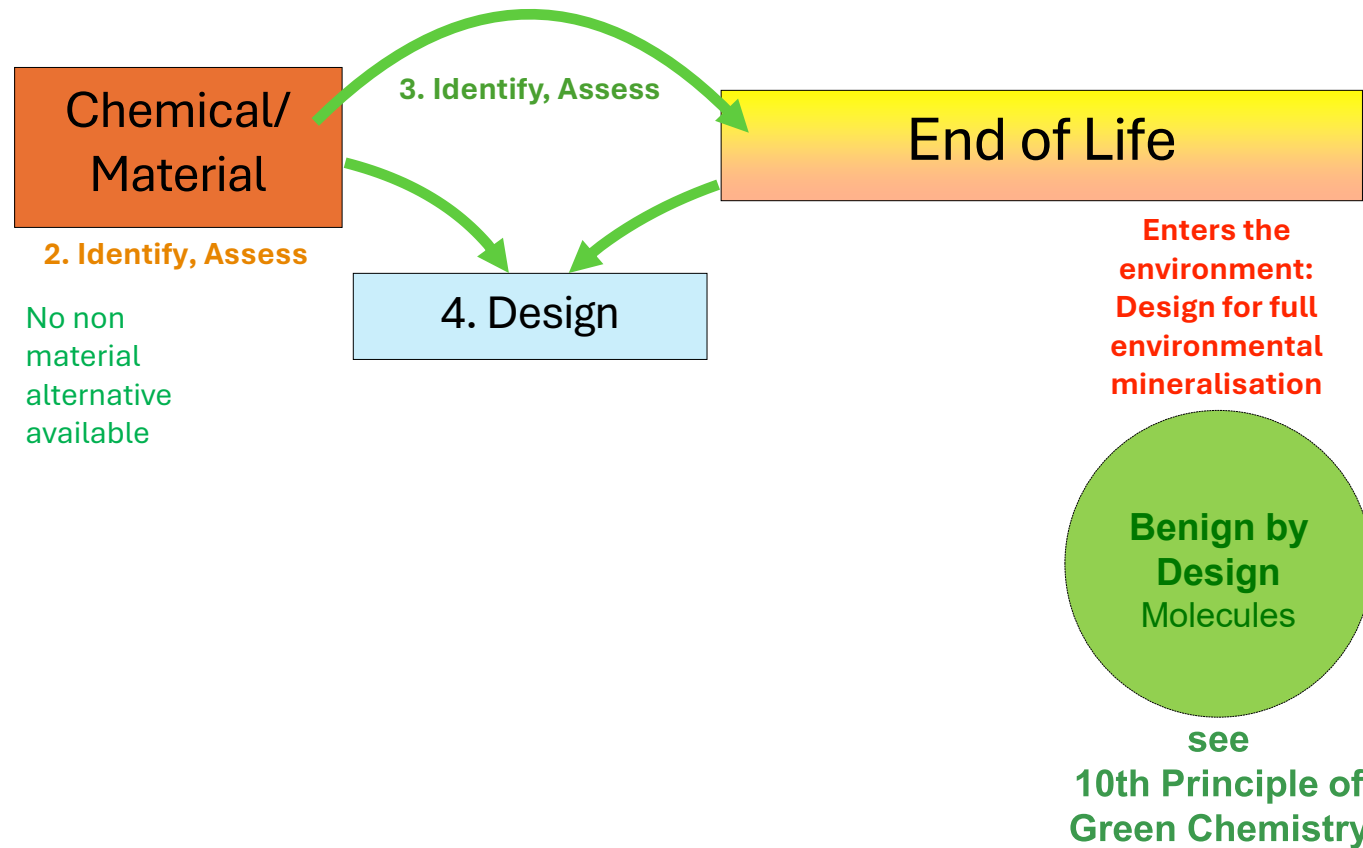
More Sustainable and Greener Pharmacy - Workflow

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



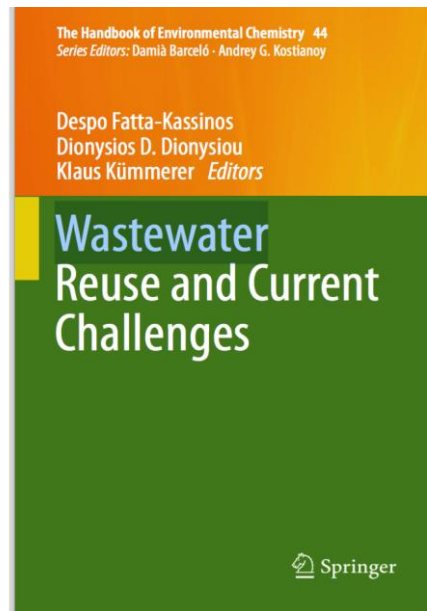
Benign by Design - Workflow

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

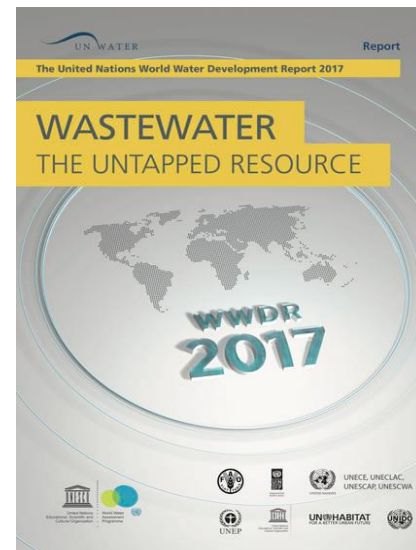


Drivers for Benign by design-Water Needs

**Increasing Need
for Water Reuse
exacerbated
by climate change**

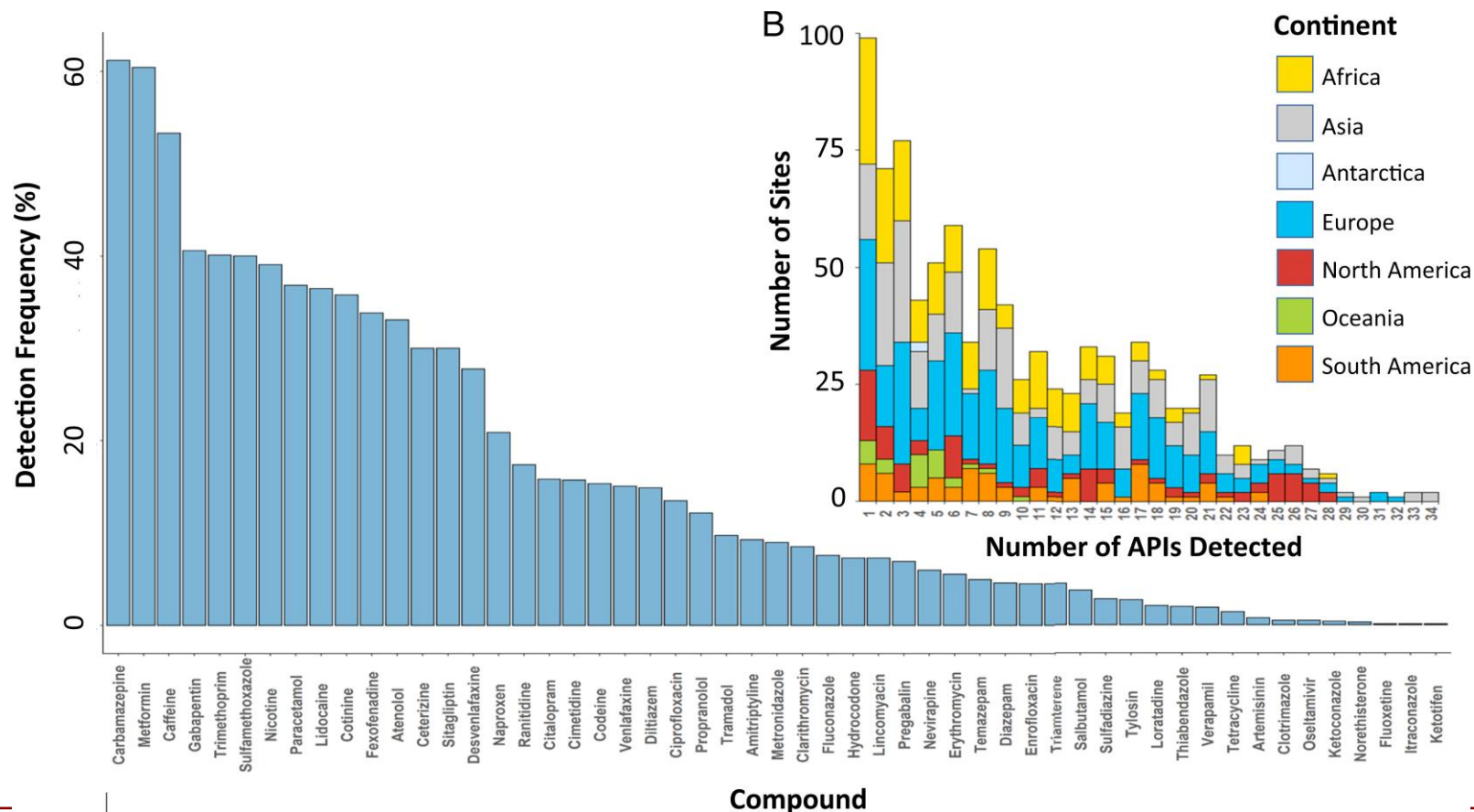


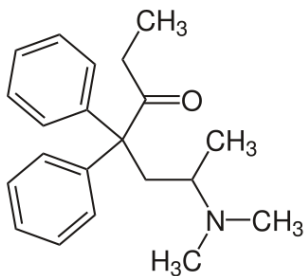
**> 80% of Waste Water
not treated (globally)**



Pharmaceuticals in Rivers Worldwide

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

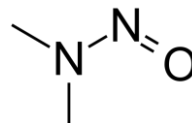




Methadone

Hanigan et al., ES&T, 2015

Chlorination



N-Nitrosodimethylamine (NDMA)

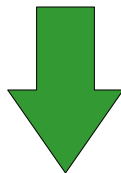
- Highly hepatotoxic
- Suspected human carcinogen
- **Threshold U.S. drinking water: 7 ng/L**

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)

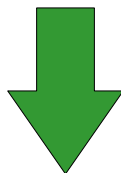
Environmental Persistence of pharmaceuticals, their metabolites and transformation products

Active Pharmaceutical Ingredients, Adjuvants, Excipients

Ready and full (bio)mineralisation in the environment



No exposure



No effects, no risk!

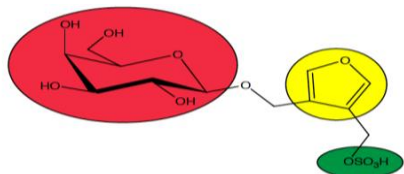
Biodegradability in the Aquatic Environment (in %) - **Without** Being Designed for it!

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



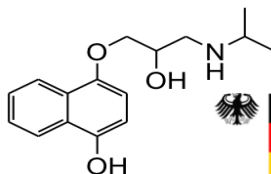
Antibiotics



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

β- Blockers



Bundesministerium
für Bildung
und Forschung

Rastogi T, Leder C, Kümmerer K (2014)
Env. Sci Technol. 111, 493–499

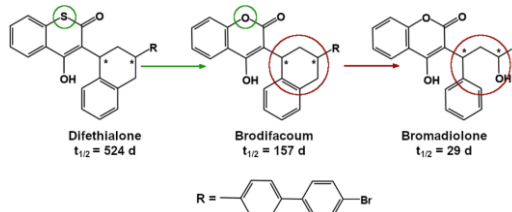
(**Propranolol**)

Rastogi T, Leder C, Kümmerer K (2014)
Chemosphere 111, 493–499

(**Metoprolol**)

Rastogi T, Leder C, Kümmerer K (2015)
RSC Adv. 5, 27, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833, 834, 835, 836, 837, 838, 839, 840, 841, 842, 843, 844, 845, 846, 847, 848, 849, 850, 851, 852, 853, 854, 855, 856, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, 873, 874, 875, 876, 877, 878, 879, 880, 881, 882, 883, 884, 885, 886, 887, 888, 889, 890, 891, 892, 893, 894, 895, 896, 897, 898, 899, 900, 901, 902, 903, 904, 905, 906, 907, 908, 909, 910, 911, 912, 913, 914, 915, 916, 917, 918, 919, 920, 921, 922, 923, 924, 925, 926, 927, 928, 929, 930, 931, 932, 933, 934, 935, 936, 937, 938, 939, 940, 941, 942, 943, 944, 945, 946, 947, 948, 949, 950, 951, 952, 953, 954, 955, 956, 957, 958, 959, 960, 961, 962, 963, 964, 965, 966, 967, 968, 969, 970, 971, 972, 973, 974, 975, 976, 977, 978, 979, 980, 981, 982, 983, 984, 985, 986, 987, 988, 989, 990, 991, 992, 993, 994, 995, 996, 997, 998, 999, 1000

Rodenticide



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

Umwelt
Bundesamt

Excipients Selection Guide

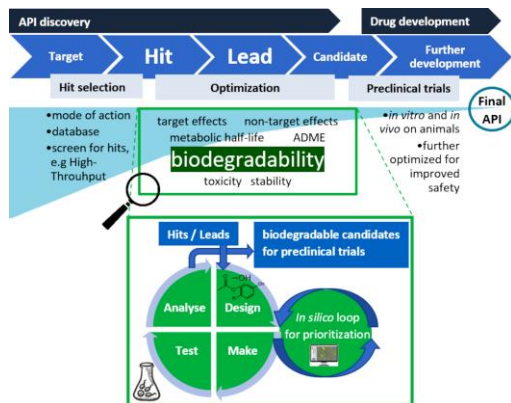


Bading, M, Griffing M., Olsson O,
Harris J, Scher J, Sakurai A,
Overcash M, Kümmerer K (2025)
Green Chemistry, 27, 15568–15581



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

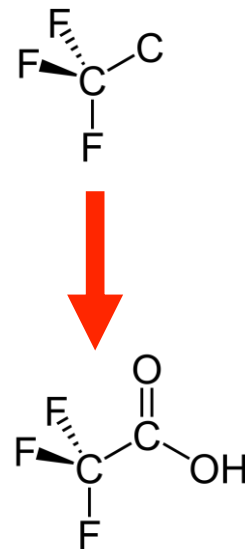
**Develop existing Design rules
further**

e.g. Assessment of Role of F

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

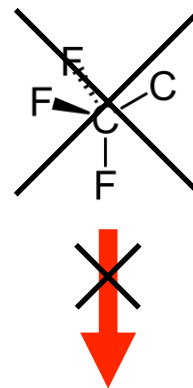
- Environmental degradation product of organic chemicals and pharmaceuticals containing

- Highly mobile, highly persistent (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**

Not in Opposition !



**Fast and full
environmental
degradation:**

- No exposure
- No effect
- No risk !



**Opportunities for
innovation and new
compounds.**

**New Businesses
Opportunities**

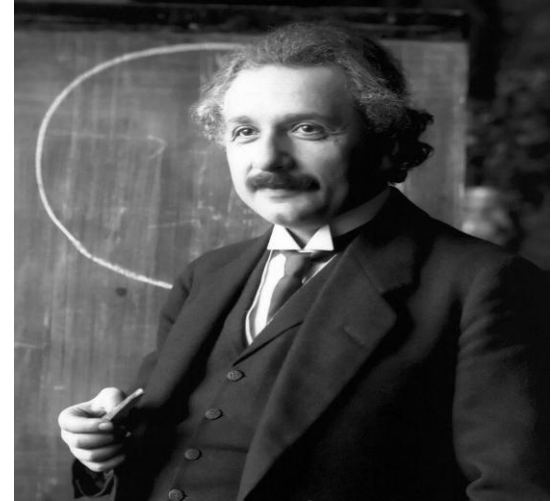


**More success stories
needed**

**Full life cycle view
necessary**

**A smart person solves a
problem.**

A wise person avoids it.



Attributed to Albert Einstein