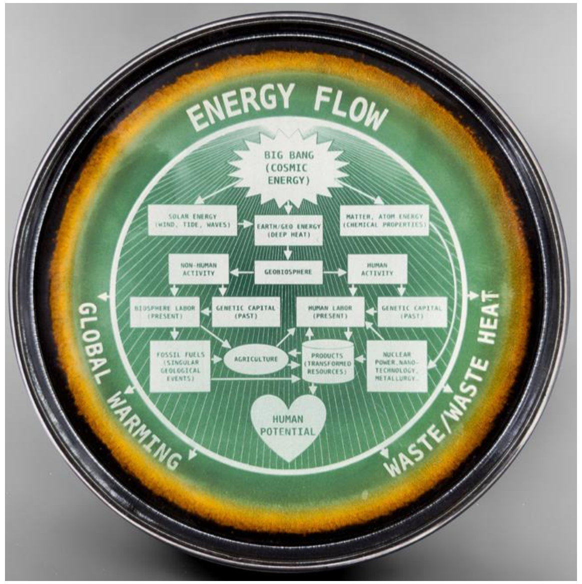
Green Metrics: Real-Life Tools & Case Study from Fragrance Industry



Solar energy flux at each stage, from its transit through the Earth's atmosphere to its absorption by photosynthetic organisms, and its use by humans

The interdependence between the economy, energy and biophysical cycles.
ecological economics pioneer N. Georgescu-Roegen

The "solar equivalent joule" to describe a terrestrial economy based on its primary energy input: the Sun.

https://disnovation.org/eatingthesun.php

Fabrice Robvieux, dsm-firmenich

Route-Scouting & Development of New Perfumery Ingredients

Education

- MSc at CPE Lyon (France)
- PhD at the University of Geneva (Prof. Peter Kündig): organometallic chemistry & Catalysis
- Post-doc at the University of Tokyo (Prof. Shu Kobayashi): Lewis base catalysis & Chemsitry in water
- Post-doc at the University of Marie-Curie (Prof. Max Malacria): radical chemistry

Career

- Firmenich SA (2004-2023)
- dsm-firmenich (2023-)
- Lecturer at the University of Geneva. Chemistry of Perfumes & Tastes (2021-)
- Course in the Catalysis & Sustainable Chemistry/Chemical engineering (Master specialization; NCCR cat.; EPFL & ETHZ) (2023-)

Bringing progress to life through our complementary business units

Perfumery & Beauty

Delivering well-being and sensory delight to consumers

Taste, Texture & Health

Converging the delicious and nutritious

Health, Nutrition & Care

Together, making our world a healthier place

Animal Nutrition & Health*

Powering the production of sustainable animal protein, transforming global food systems for good

*To be separated out over the course of 2025

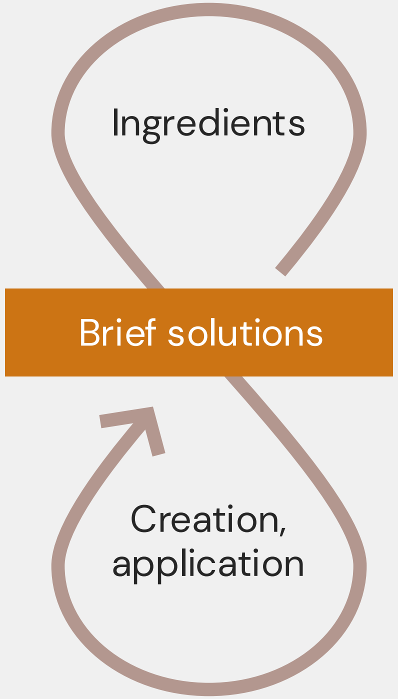
Co-creation with our customers to achieve what consumers want

Sustainability as business driver

Ingredient toolbox

Excellence in portfolio, quality-breadth and regulation

- **Synthetics**
- **Biotechnology**
- **Naturals**



Creation & Innovation

Best-in-class customer intimacy, consumer insights and technical application expertise

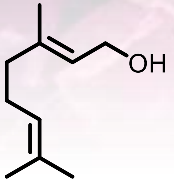
Science & Research Innovation

dsm-firmenich

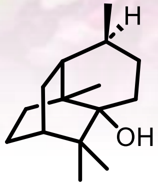
Fragrance – an unique equation

Natural extracts

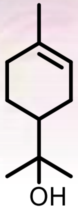
Flower or fruit extraction



Geraniol
(Rose)

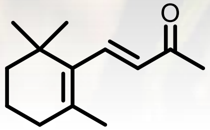


Patchoulol
(Earthy)

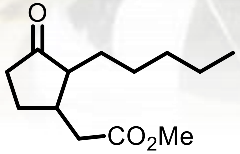


α-Terpineol
(Floral)

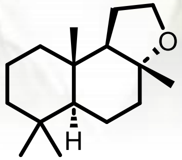
Nature identicals



β-Ionone
(Violet)

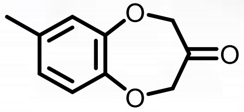


Hedione®
(Jasmine)

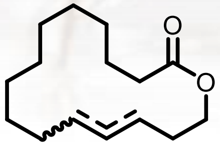


Ambrox® Super
(Amber)

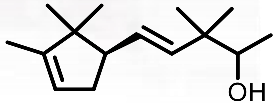
Synthetics



Calone®
(Watery)



Habanolide®
(Musk)



Polysantol®
(Sandalwood)

Green Metrics: Real-Life Tools & Case Study from Fragrance Industry

Goal of the course

Provide a comprehensive perspective of the green metrics developed, used in the chemical industries. The pros/cons and the limitations of all these metrics will be shown as well as the different need between industries. The case of Perfumery industry will be specially emphasized.

Course Syllabus

- Green Chemistry & Sustainability
- Presentation of the different metrics
- Pros/Cons & Limitations
- What is the purpose of these metrics?
- Presentation of different methodologies
- Difference between the pharma industry and Perfumery industry
- Example in the Perfumery industry: Ecoscent Compass, Green Motion or Estée Lauder Companies

fabrice.robvieux@dsm-firmenich.com
Associate Principal Scientist, dsm-firmenich

www.dsm-firmenich.com

Green Metrics: Real-Life Tools

Green Chemistry, Sustainable Chemistry? Why ?

Boundaries? Limits? System Thinking?

Metric(s)?
How many?
What kind?
Data Availability? Accuracy?
Why are they needed?
What’s next?

Sustainable Development Goal (2015-2030)? After 2030?

What are the Potential Pitfalls?

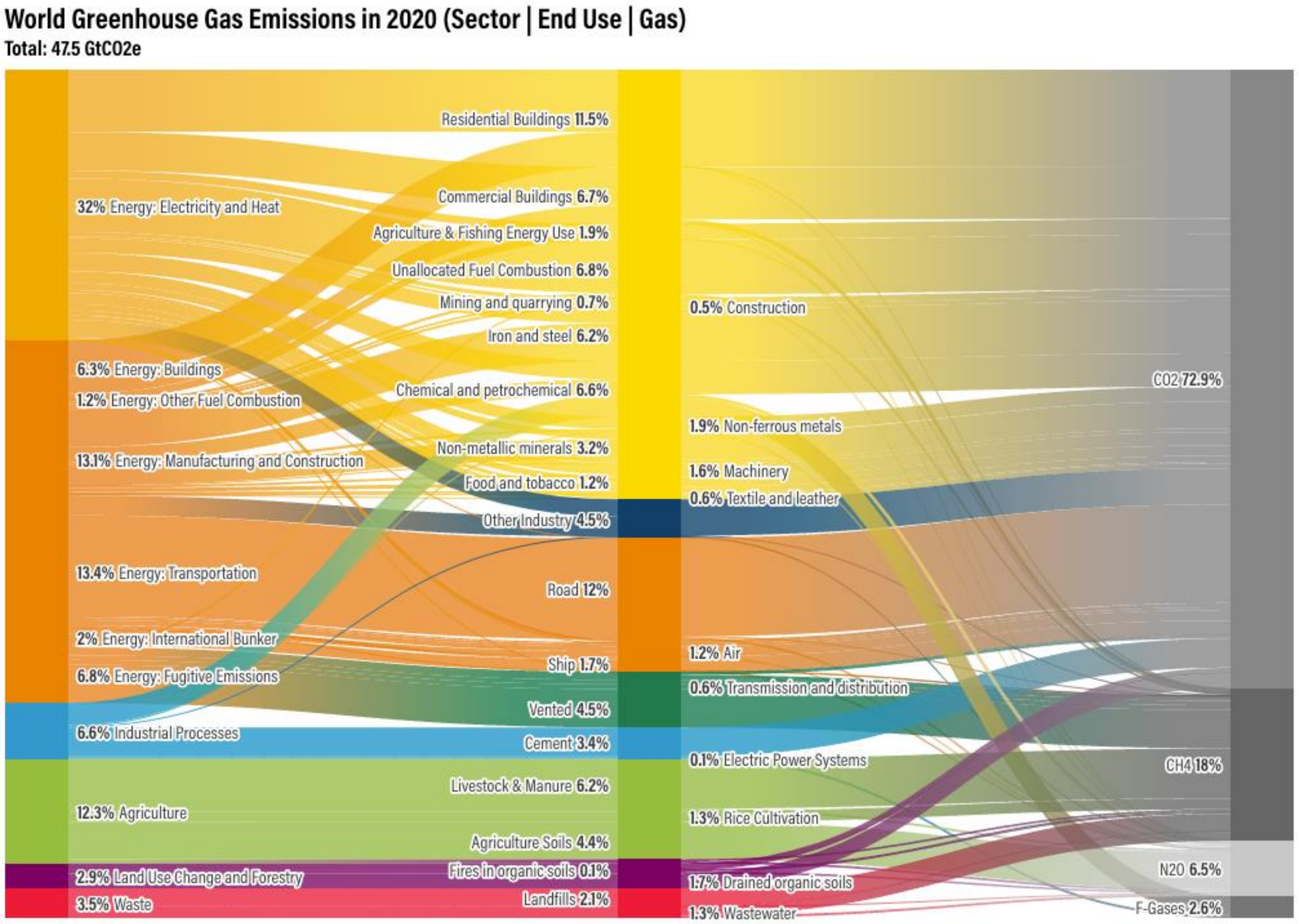
Planetary Boundaries – Holocene – Anthropocene?

Where do we stand?

Do Limits exist?

Have they been reached?

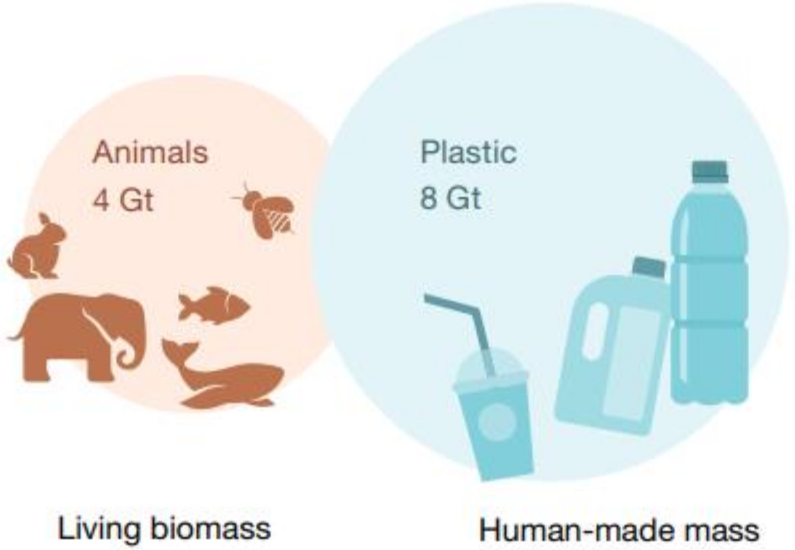
Greenhouse Emissions



Past estimation: 49,8 $GtCO_2e$ (2019)

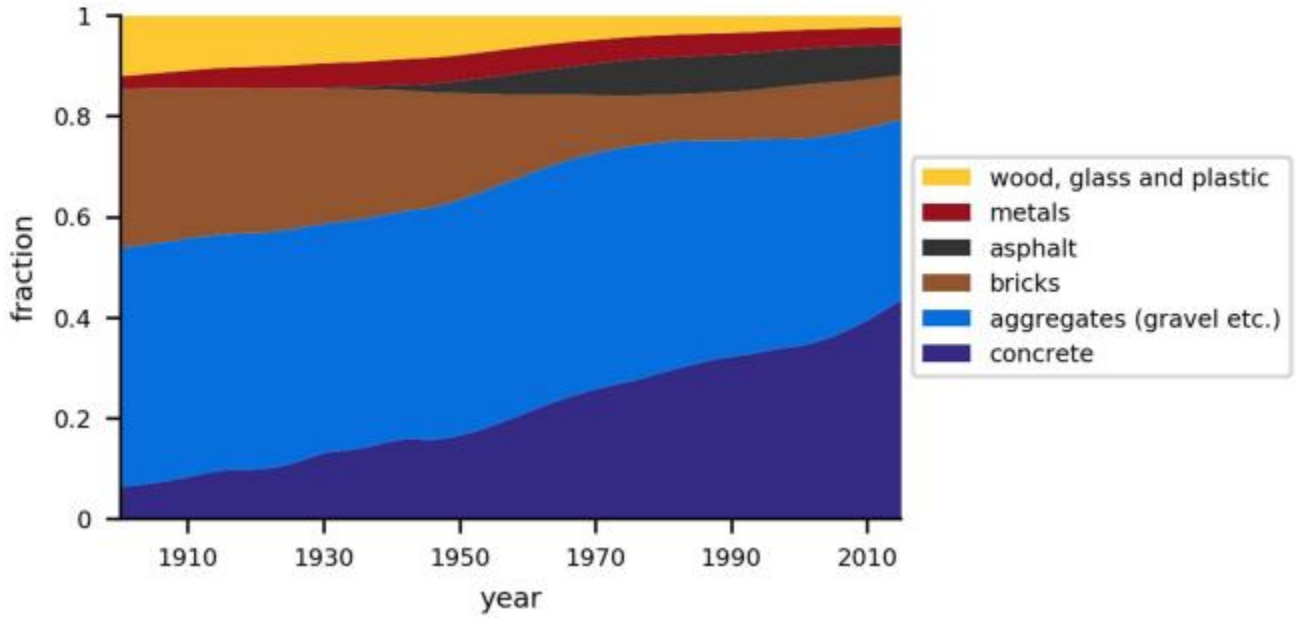
Holocene -Anthropocene

Biomass vs Human-made mass?



Nature **2020**, *588*, 442.
https://doi.org/10.1038/s41586-020-3010-5

Holocene -Anthropocene

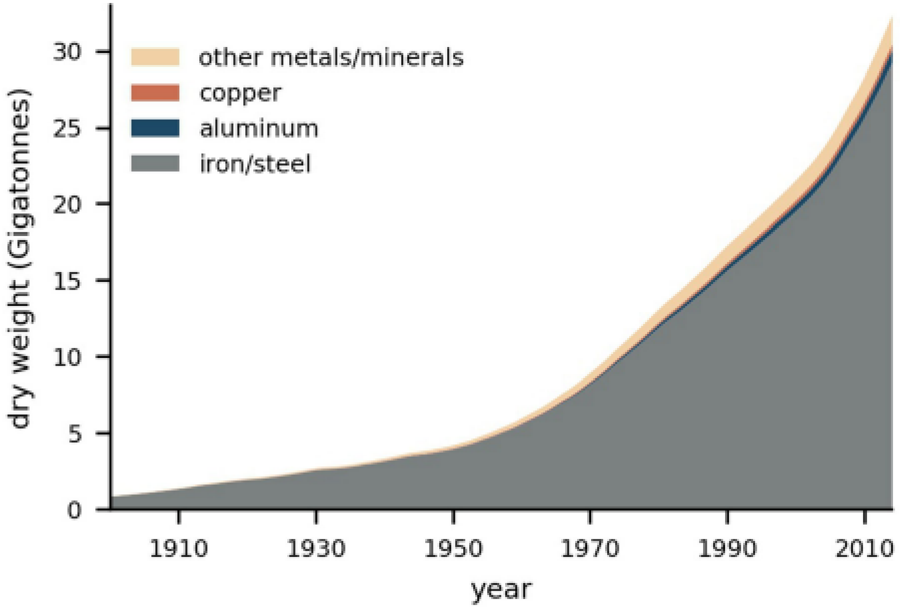


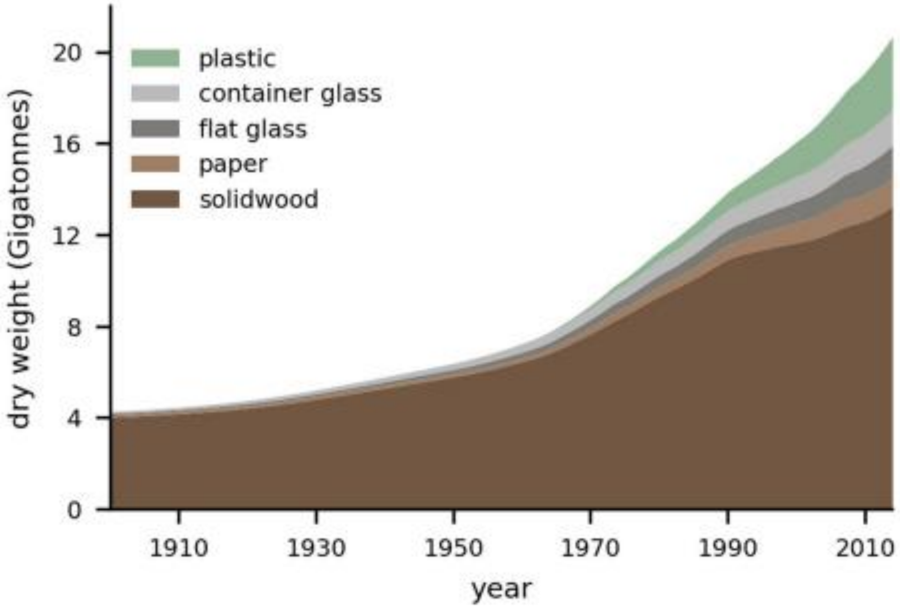
Anthropogenic mass composition since the year 1900, divided into material groups

Nature **2020**, *588*, 442.
https://doi.org/10.1038/s41586-020-3010-5

Krausmann, F., Lauk, C., Haas, W. & Wiedenhofer, D. From resource extraction to outflows of wastes and emissions: the socioeconomic metabolism of the global economy, 1900–2015.
Glob. Environ. Change **2018**, *52*, 131–140.

Holocene -Anthropocene

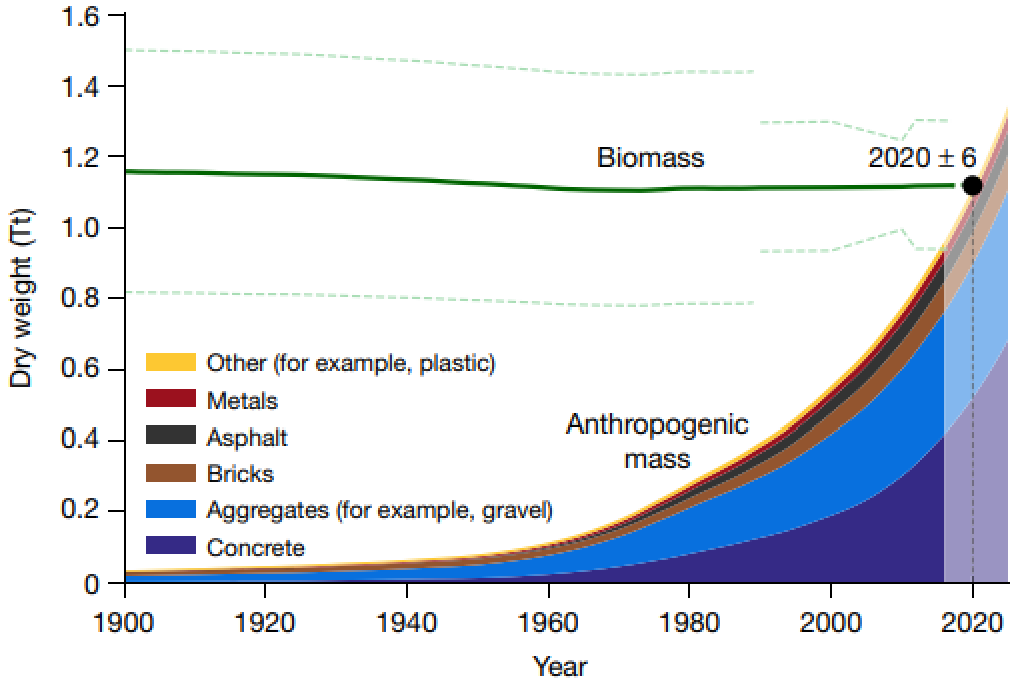




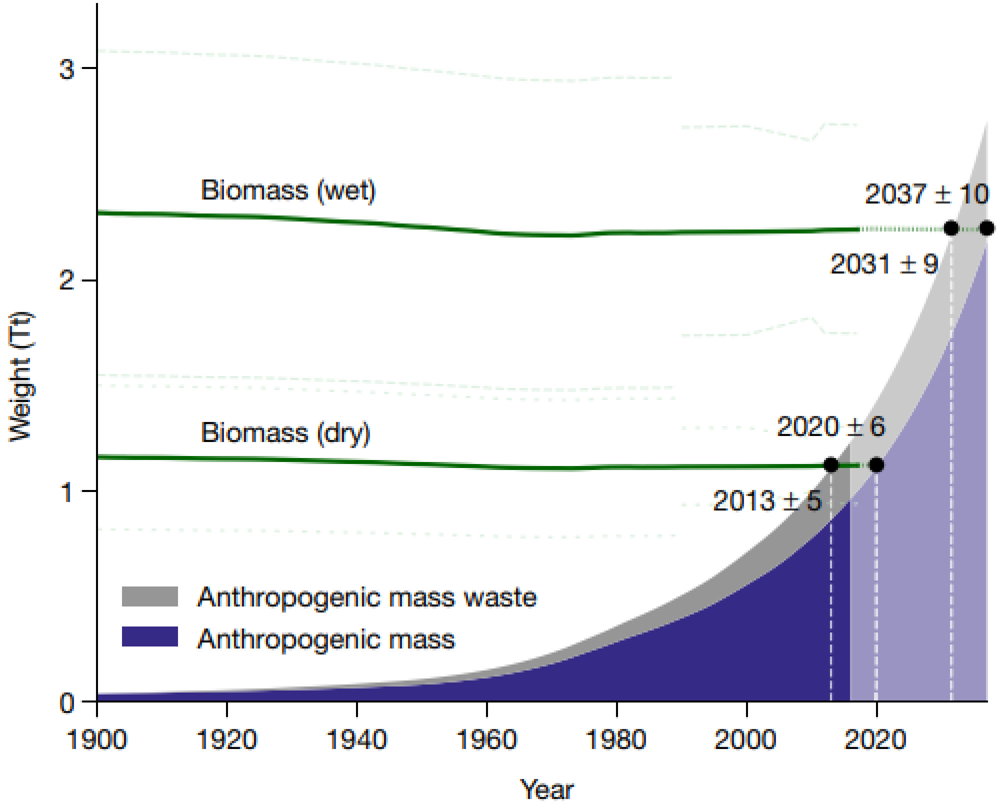
Nature **2020**, *588*, 442.
https://doi.org/10.1038/s41586-020-3010-5

Holocene -Anthropocene

Biomass dry



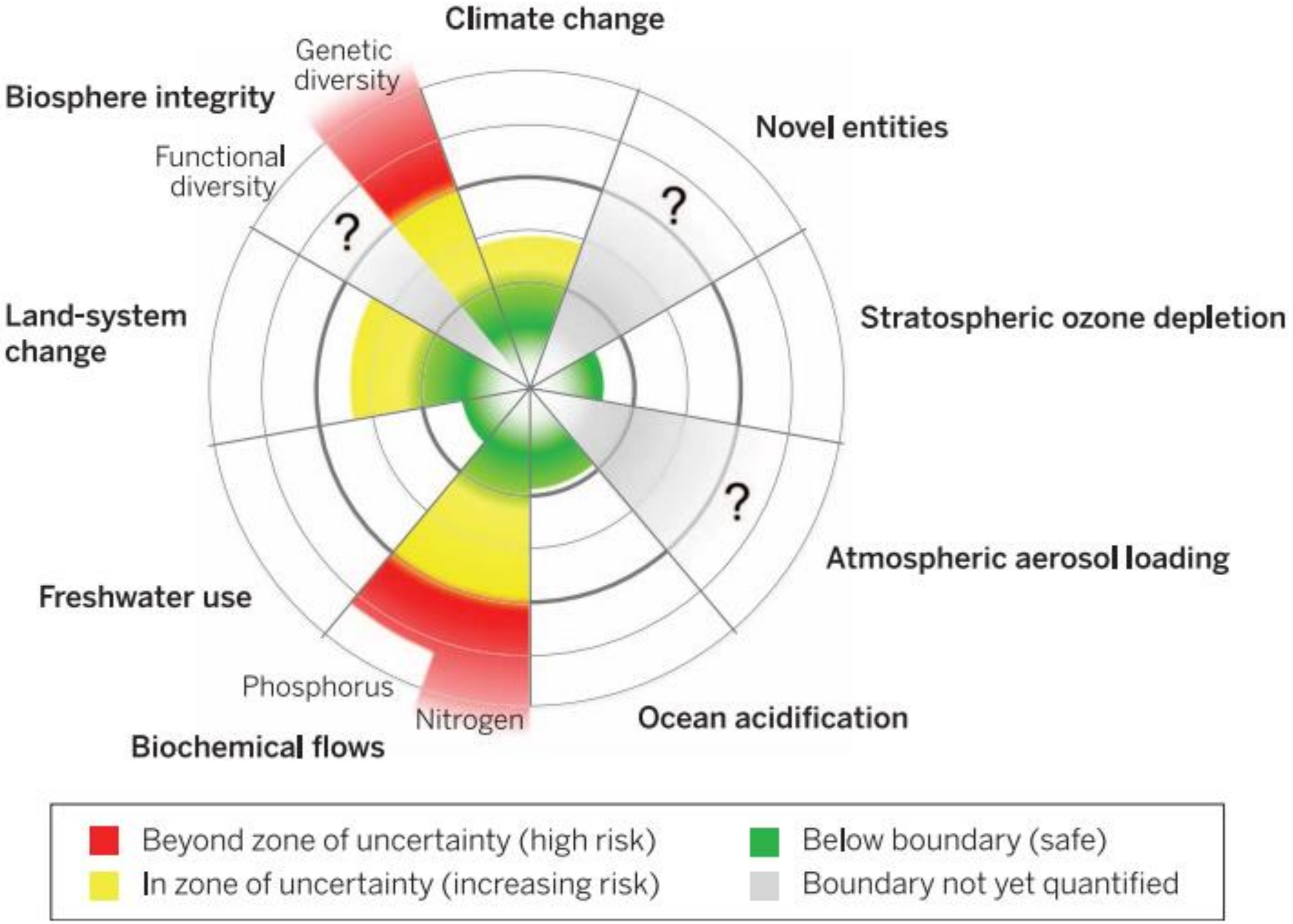
Dashed green lines: ±1 s.d.



Nature **2020**, *588*, 442.
https://doi.org/10.1038/s41586-020-3010-5

Planetary Boundaries

What does that means?



Science **2015**, *347*, 1259855.
DOI: 10.1126/science.1259855

https://planetaryboundaries.kcvs.ca/

Planetary Boundaries

Rockström, J. *et al.*,
Planetary boundaries: Exploring the safe operating space for humanity.
Ecol. Soc. **2009**, *14*, 32.
http://www.ecologyandsociety.org/vol14/iss2/art32/
Rockström, J. *et al.*, A safe operating space for humanity. *Nature* **2009**, *461*, 472.
http://dx.doi.org/10.1038/461472a

PLANETARY BOUNDARIES

Earth-system process	Parameters	Proposed boundary	Current status	Pre-industrial value
Climate change	(i) Atmospheric carbon dioxide concentration (parts per million by volume)	350	387	280
	(ii) Change in radiative forcing (watts per metre squared)	1	1.5	0
Rate of biodiversity loss	Extinction rate (number of species per million species per year)	10	>100	0.1–1
Nitrogen cycle (part of a boundary with the phosphorus cycle)	Amount of N_2 removed from the atmosphere for human use (millions of tonnes per year)	35	121	0
Phosphorus cycle (part of a boundary with the nitrogen cycle)	Quantity of P flowing into the oceans (millions of tonnes per year)	11	8.5–9.5	-1
Stratospheric ozone depletion	Concentration of ozone (Dobson unit)	276	283	290
Ocean acidification	Global mean saturation state of aragonite in surface sea water	2.75	2.90	3.44
Global freshwater use	Consumption of freshwater by humans (km^3 per year)	4,000	2,600	415
Change in land use	Percentage of global land cover converted to cropland	15	11.7	Low
Atmospheric aerosol loading	Overall particulate concentration in the atmosphere, on a regional basis	To be determined		
Chemical pollution	For example, amount emitted to, or concentration of persistent organic pollutants, plastics, endocrine disrupters, heavy metals and nuclear waste in, the global environment, or the effects on ecosystem and functioning of Earth system thereof	To be determined		

Planetary Boundaries

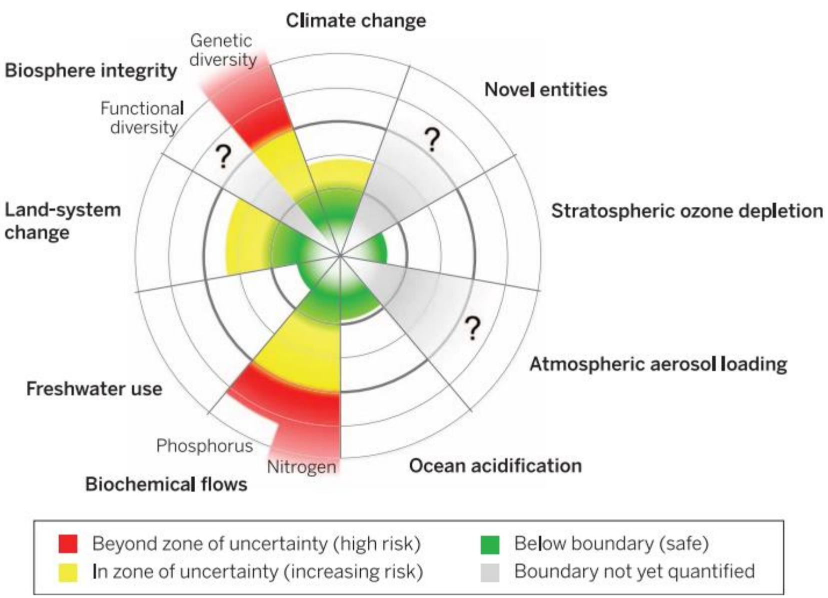
Earth-system process	Control variable(s)	Planetary boundary (zone of uncertainty)	Current value of control variable
Climate change (R2009: same)	Atmospheric CO_2 concentration, ppm	350 ppm CO_2 (350–450 ppm)	398.5 ppm CO_2
	Energy imbalance at top-of-atmosphere, W m^{-2}	+1.0 W m^{-2} (+1.0–1.5 W m^{-2})	2.3 W m^{-2} (1.1–3.3 W m^{-2})
Change in biosphere integrity (R2009: Rate of biodiversity loss)	*Genetic diversity:* Extinction rate	< 10 E/MSY (10–100 E/MSY) but with an aspirational goal of ca. 1 E/MSY (the background rate of extinction loss). E/MSY = extinctions per million species-years	100–1000 E/MSY
	Functional diversity: Biodiversity Intactness Index (BII) Note: These are interim control variables until more appropriate ones are developed	Maintain BII at 90% (90–30%) or above, assessed geographically by biomes/large regional areas (e.g. southern Africa), major marine ecosystems (e.g., coral reefs) or by large functional groups	84%, applied to southern Africa only

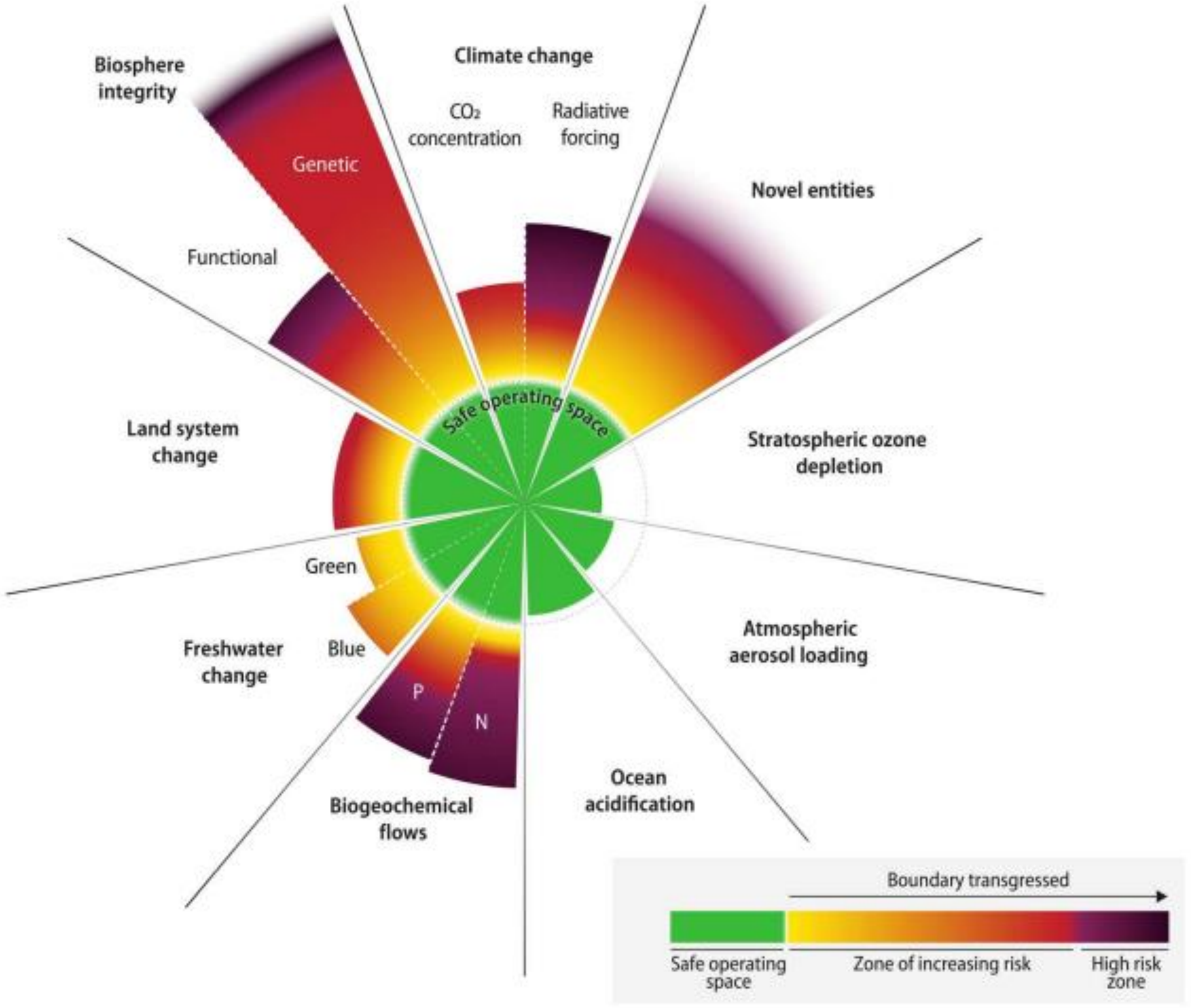
Science **2015**, *347*, 1259855.
DOI: 10.1126/science.1259855

https://www.co2.earth/daily-co2

Planetary Boundaries

What does that means?



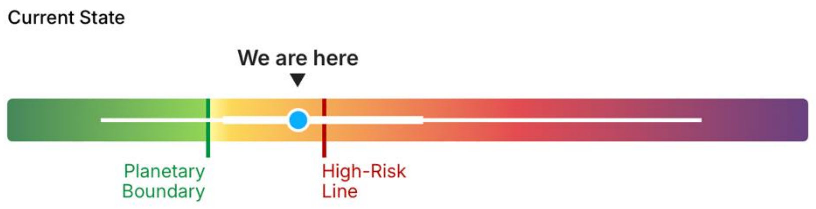


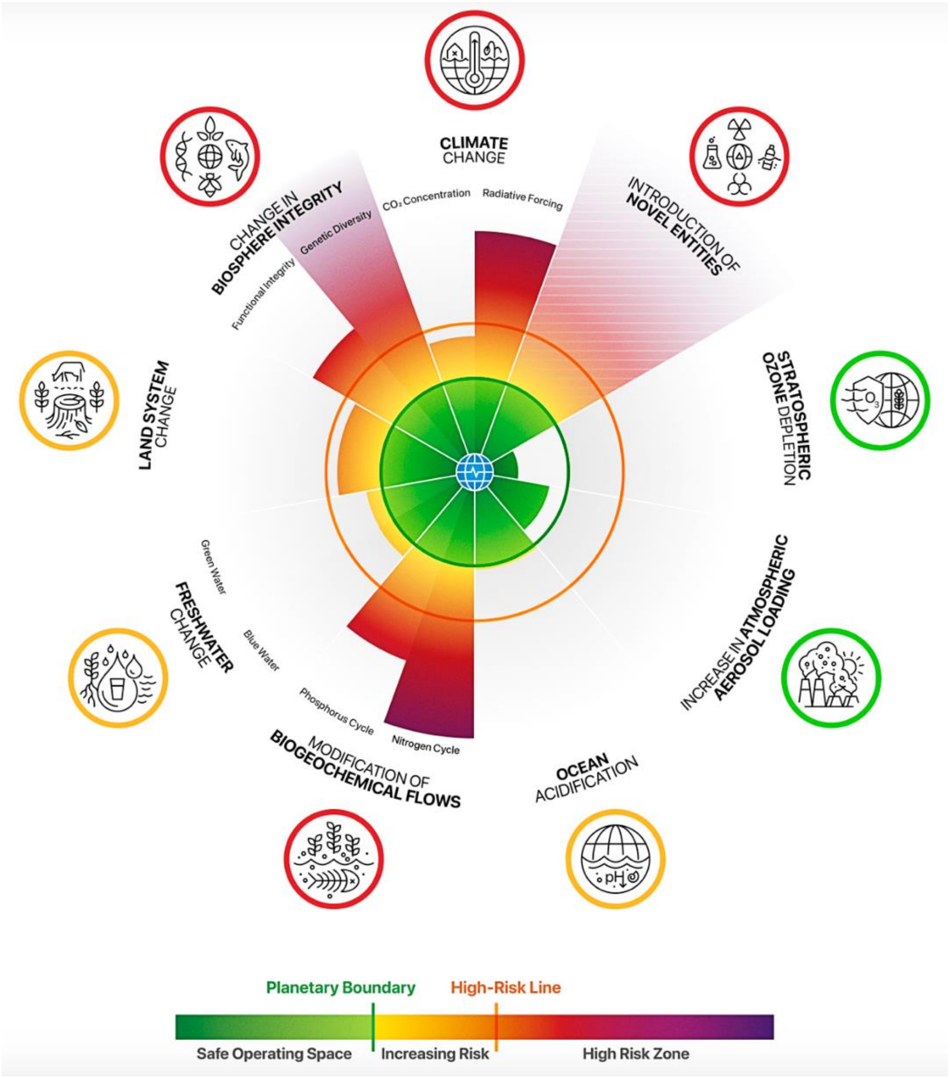
Science Adv. **2023**, eadh2458.
https://doi.org/10.1126/sciadv.adh2458

Planetary Boundaries

Where do we stand?

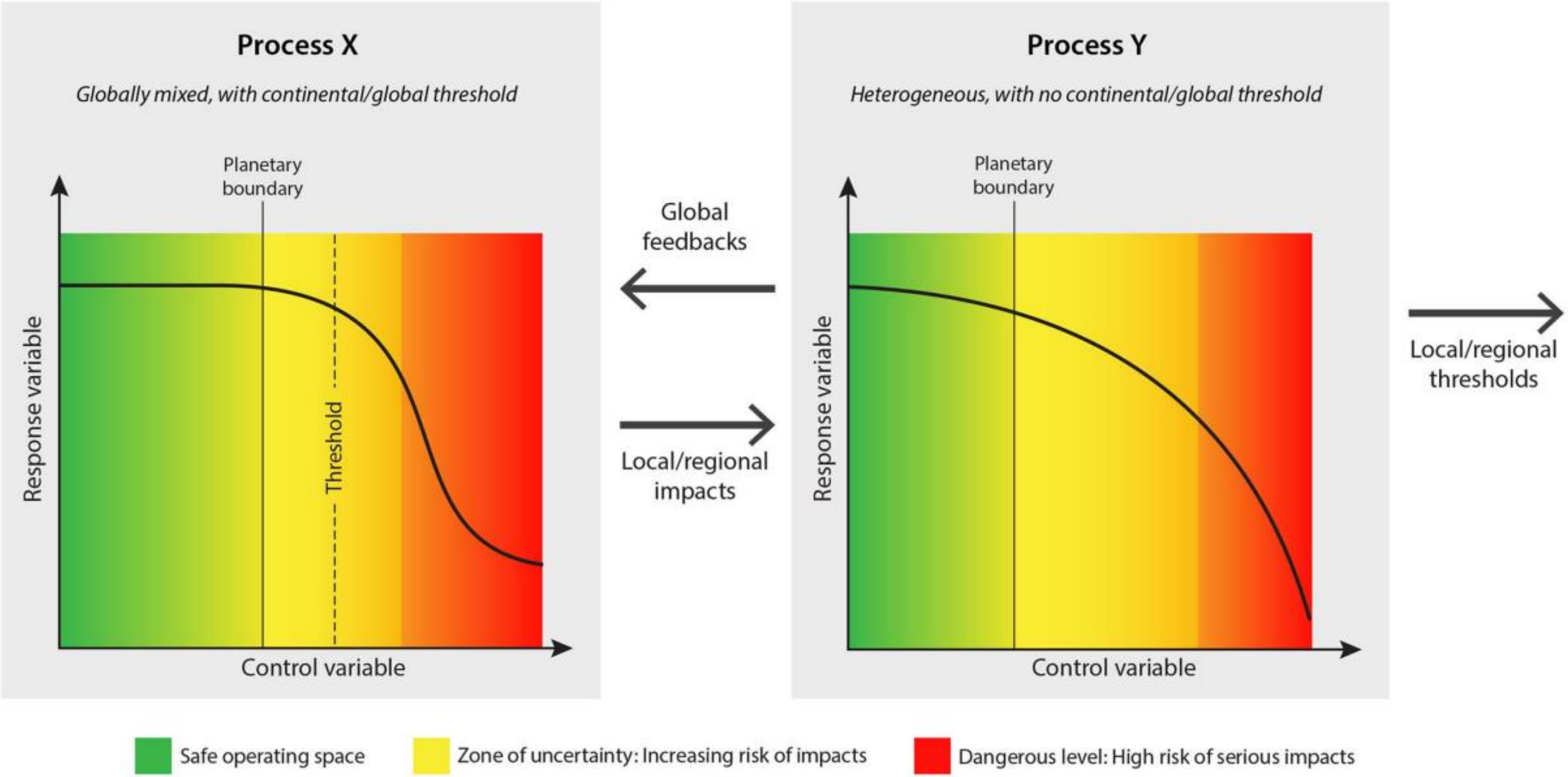
POTSDAM INSTITUTE FOR CLIMATE IMPACT RESEARCH





https://www.planetaryhealthcheck.org

Planetary Boundaries



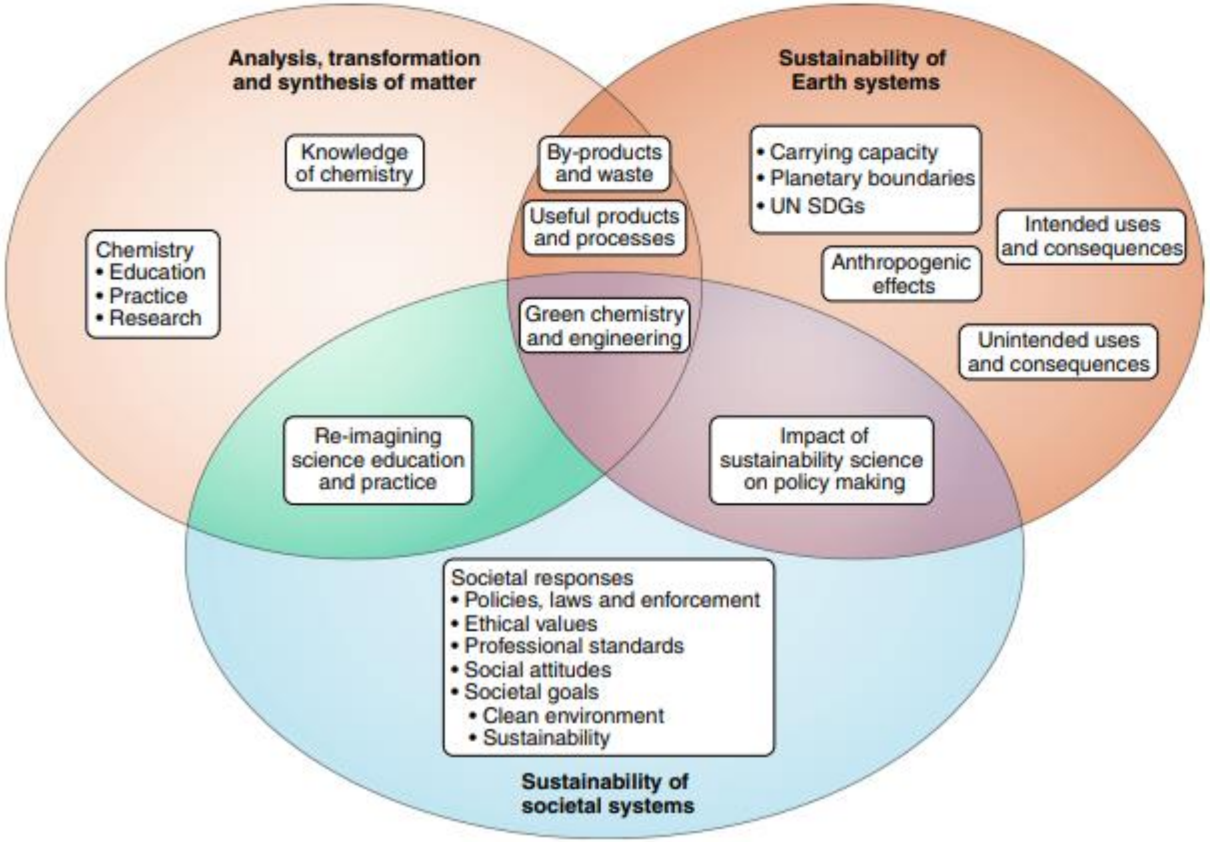
Science **2015**, *347*, 1259855.
DOI: 10.1126/science.1259855

Systems Thinking

“The ability to understand and interpret complex systems” and involves: “visualizing the interconnections and relationships between the parts in the system; examining behaviors that change over time; and examining how systems-level phenomena emerge from interactions between the system’s parts”

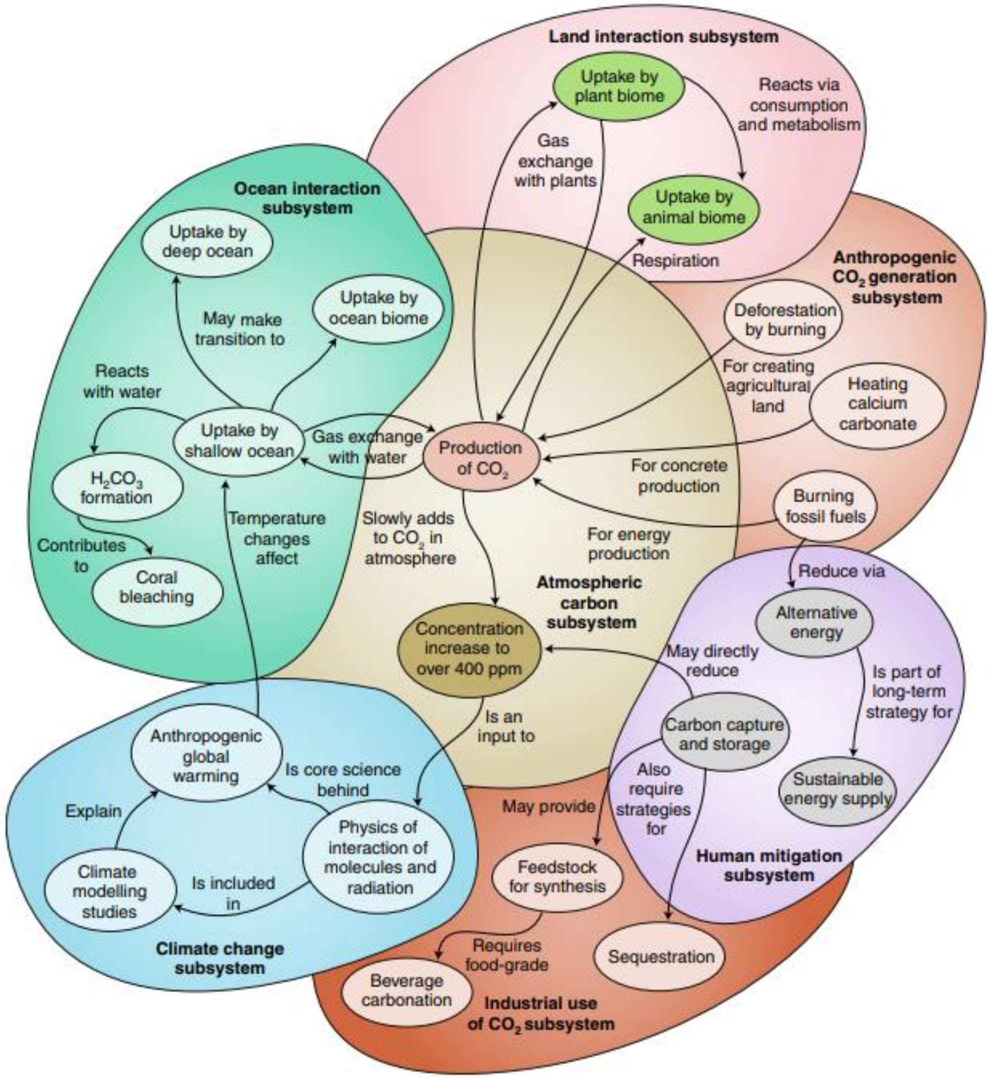
https://iupac.org/project/2020-014-3-050/

Systems Thinking



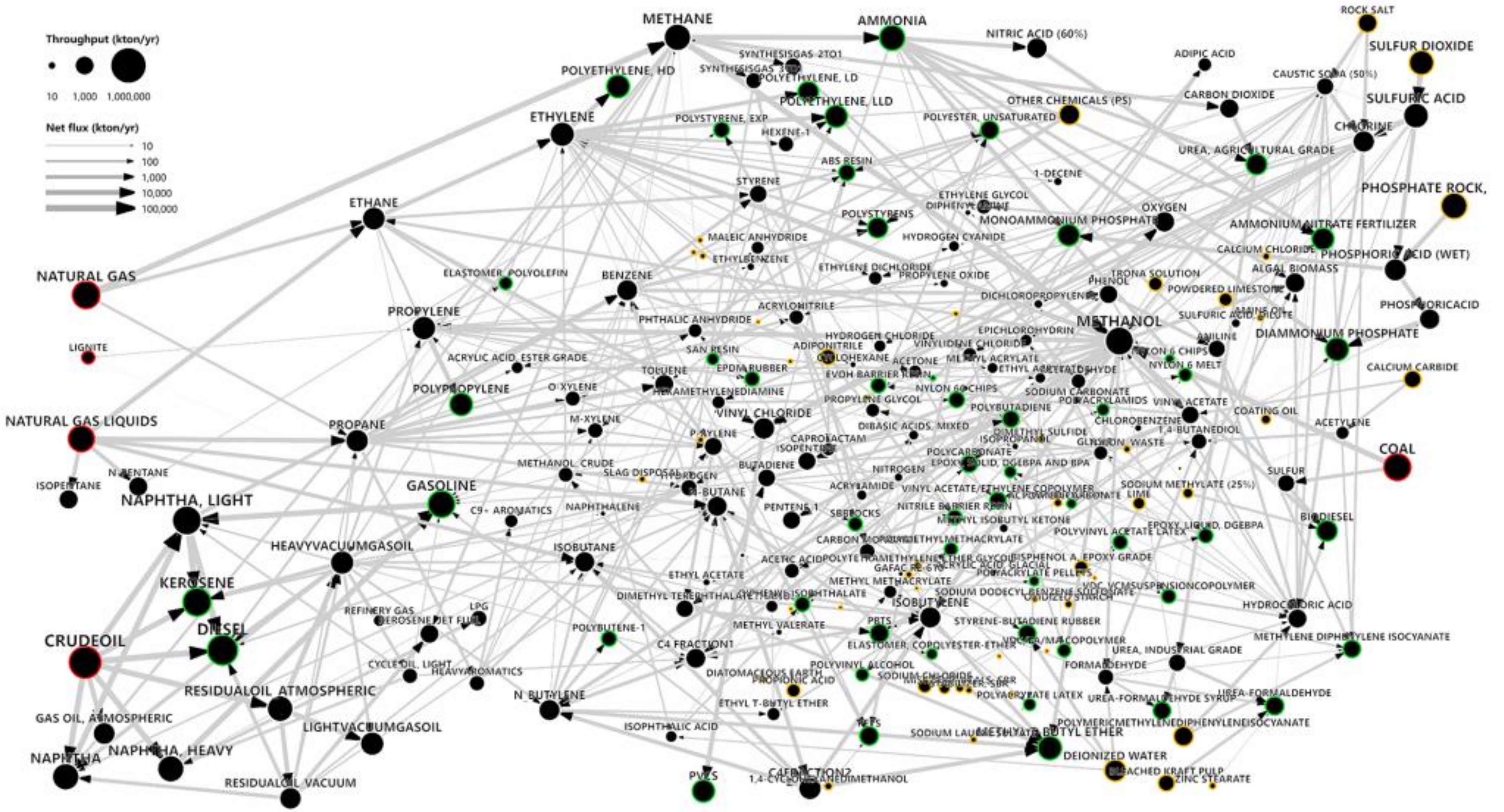
Mahaffy, P. G. & *al. Nature Sustainability* **2019**, *2*, 362.

Systems Thinking



Mahaffy, P. G. & *al. Nature Sustainability* **2019**, *2*, 362.

Systems Thinking

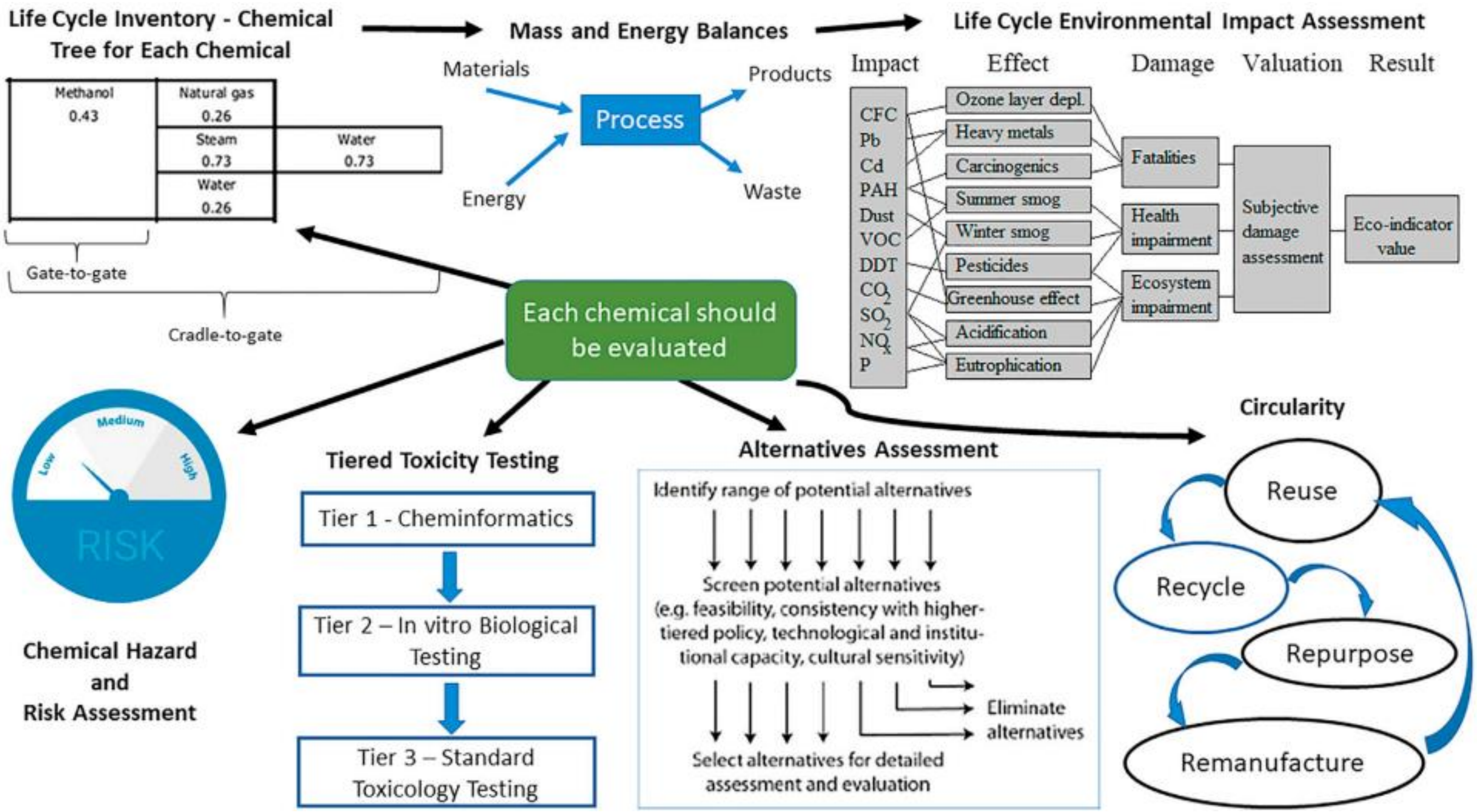


Chem Z. *et al.* *ACS Sus. Chem. Eng.*, **2023**, ASAP
https://doi.org/10.1021/acssuschemeng.3c00990

Systems Thinking

Constable, D. J. C. *iScience* **2021**, *24*, 103489.
https://doi.org/10.1016/j.isci.2021.103489

Systems Thinking



Constable, D. J. C. *iScience* **2021**, *24*, 103489.
https://doi.org/10.1016/j.isci.2021.103489

Green Metrics: Real-Life Tools

Green Chemistry

WHY ? DEFINITION?

Green Chem. **2001**, *10*, 1274.

Green Metrics: Real-Life Tools

Green Chemistry has been defined as the use of chemistry for pollution prevention using suitable designs of products and processes, reducing and mainly, if possible, eliminating the use and generation of hazardous substances.

Anastas & Warner stated in 1998: «It is an approach that provides a fundamental methodology for changing the intrinsic nature of a chemical product or process so that it is inherently of less risk to human and the environment, to prevent pollution, and thereby solve environmental problems, promoting pollution prevention and industrial ecology»

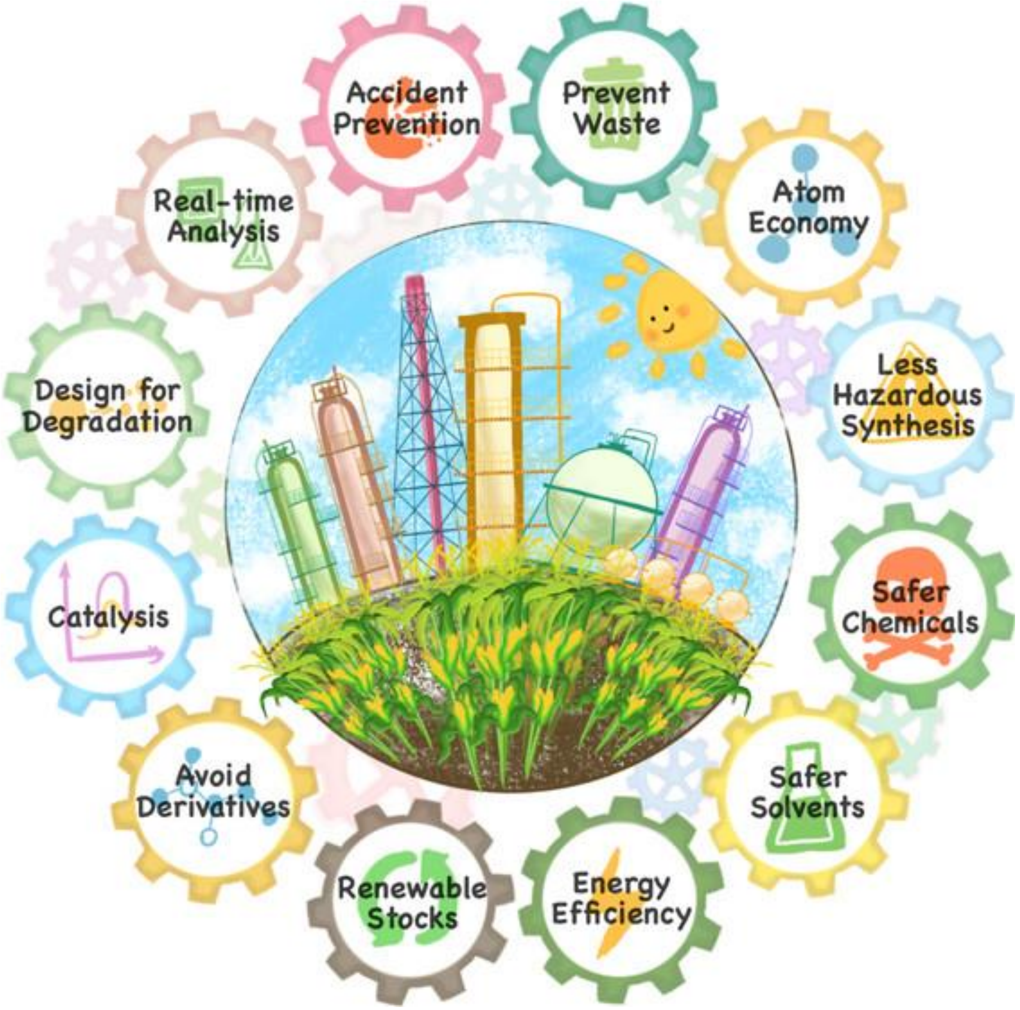
Noyori expressed that "green chemistry is not just a catchphrase. It is an indispensable principle of chemical research that will sustain our civilized society in the twenty-first century and further into the future."

Anastas, P.T.; Warner, J.C. Green Chemistry: Theory and Practice; Oxford University Press: Oxford, UK, **1998**.
Noyori, R. Synthesizing Our Future, *Nat. Chem.*, **2009**, *1*, 5–6.
Processes **2022**, *10*, 1274.
https://doi.org/10.3390/pr10071274

Anastas, P.; Zimmerman, J. B. *Chem.* **2016**, *1*, 10−12.
Mahaffy, P. G.; Matlin, S. A.; Holme, T. A.; MacKellar, J. *Nat. Sustain.* **2019**, *2*, 362-370.

Green Metrics: Real-Life Tools

Green Chemistry: 12 Principles



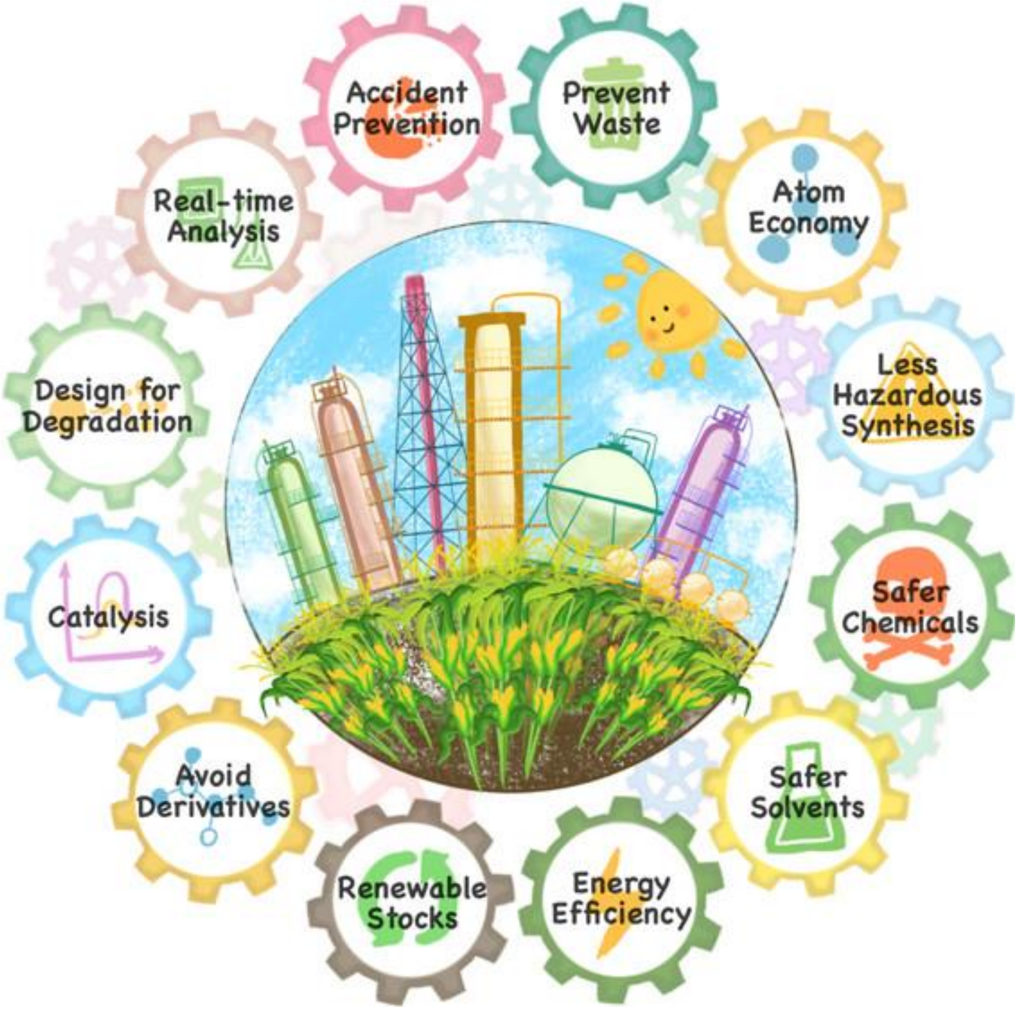
Anastas, P. T.; Eghbali, N. Green Chemistry: Principles and Practice. *Chem. Soc. Rev*. **2010**, *39*, 301.
Whiteker, G. T. *Org. Process Res. Dev.* **2019**, *23(10)*, 2109−2121.

Green Metrics: Real-Life Tools

Green Chemistry: 12 Principles

Condensed Principles of Green Chemistry

P - Prevent wastes
R - Renewable materials
O - Omit derivatization steps
D - Degradable chemical products
U - Use safe synthetic methods
C - Catalytic reagents
T - Temperature, Pressure ambient
I - In-Process Monitoring
V - Very few auxiliary substances
E - E-factor, maximise feed in product
L - Low toxicity of chemical products
Y - Yes, it is safe



Tang, S. M. L.; Smith, R. L.; Poliakoff, M. *Green Chem*., **2005**, *7*, 761.

Green Metrics: Real-Life Tools

Sustainable Chemistry is engaged toward the life cycle assessment (LCA), which is associated with the entire life cycle of a product, process, or activity.

OECD's definition: *"Sustainable chemistry is a scientific concept that seeks to improve the efficiency with which natural resources are used to meet human needs for chemical products and services. Sustainable chemistry encompasses the design, manufacture and use of efficient, effective, safe and more environmentally benign chemical products and processes."*

Benefits of Sustainable Chemistry

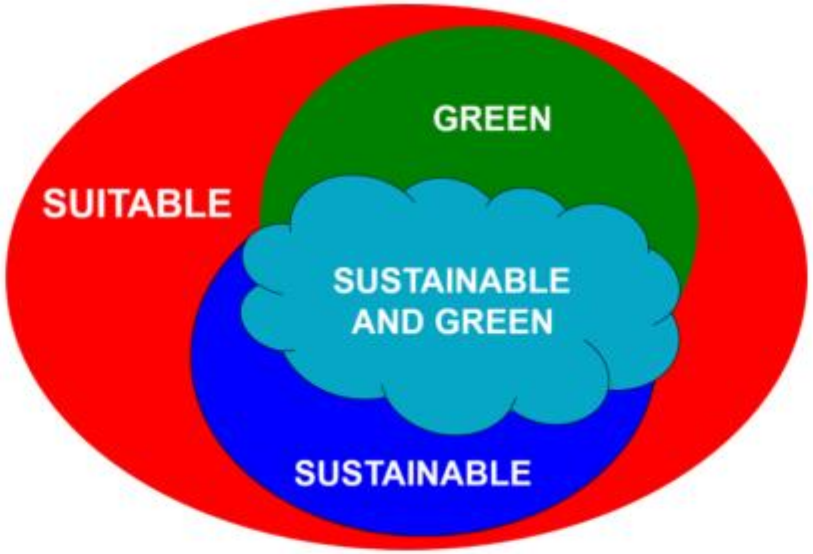
The **environmental** and **societal** benefits of sustainable chemistry include:

- Avoiding the use of persistent, bioaccumulative, toxic, and otherwise hazardous materials,
- Using renewable resources and decreasing consumption of non-renewable resources,
- Minimising negative environmental impacts of chemical processing and manufacturing,
- Providing technologies that are economically competitive for and advantageous to industry.

OECD Sustainable Chemistry.
Krasnodębski, M. An unlikely bifurcation: history of sustainable (but not Green) chemistry. *Found Chem* (2023).
https://doi.org/10.1007/s10698-023-09474-x

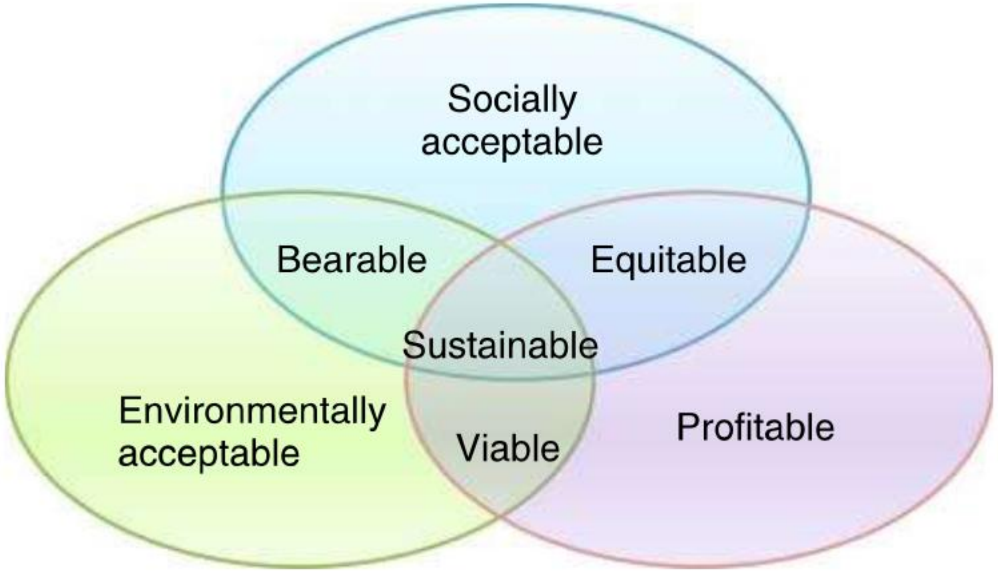
Green Metrics: Real-Life Tools

Green Chemistry & Sustainable Chemistry



Horvàth I. T. *Chem. Rev*. **2018**, *118*, 369.

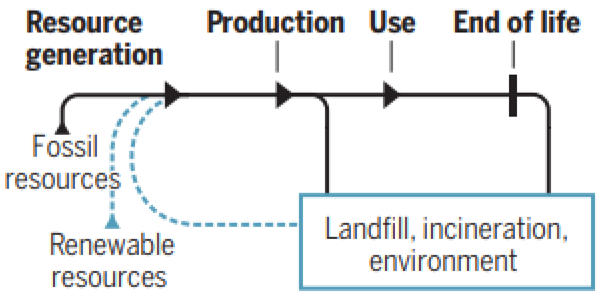
Sustainability various faces: economic, social & environmental



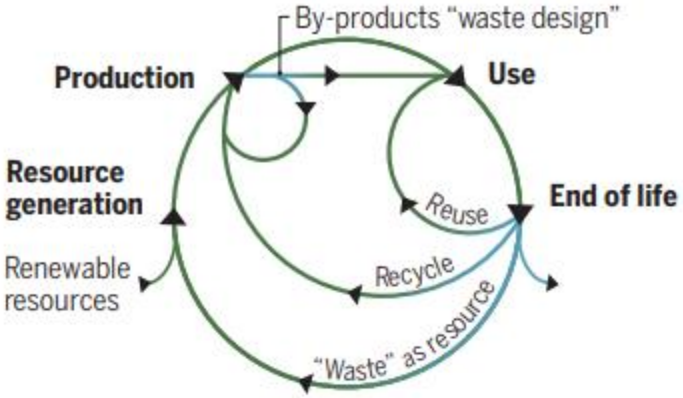
Sustainable Flow Chemisty, Ed. Wiley, **2025**.

Designing

Today's chemical sector



Tomorrow's chemical sector



Today		Tomorrow
Mostly linear processes	→	Circular processes
Fossil feedstocks	→	Renewable feedstocks
Reactive, persistent, or toxic chemical reagents and products	→	Benign chemical reagents and products
Catalysis using rare metals	→	Catalysis using abundant metals, enzymes, photons, or electrons
Covalent bonds	→	Weak, noncovalent interactions
Conventional solvents	→	Low toxicity, recyclable, inert, abundant, easily separable green solvents or solventless
Material- and energy-consuming isolation and purification	→	Self-separating systems
Large "waste" volume	→	Atom-, step-, and solvent-economical processes
"Waste" treatment	→	"Waste" utilization
Design exclusively for use phase with reliance on circumstantial control	→	Intentional molecule design for full life cycle
Performance = maximize function	→	Performance = maximize function + minimize hazards
Maximum chemical production for increased profit	→	Maximum performance with minimal benign material use for increased profit

Zimmerman, J. B. *et al. Science*. **2020**, *397*, 397-400.

The Molecular Basis of Sustainability

Chemistry as a central domain

Chemists have been responsible for deeply understanding the material world and how it functions.
Paradigm shift is needed

Box 1. Examples Contrasting Green Chemistry Principles with Traditional Chemical Approaches

Principle 1: avoid waste
Traditional: waste is something to be managed, measured, treated, and disposed of

Principle 3: reagents should be non-toxic
Traditional: toxic chemicals can be safely managed through circumstantial controls

Principle 5: feedstocks should be renewable
Traditional: chemical feedstocks are derived from finite and depleting sources

Anastas, P.; Zimmerman, J. B. *Chem.* **2016**, *1*, 10–12.
Mahaffy, P. G.; Matlin, S. A.; Holme, T. A.; MacKellar, J. *Nat. Sustain.* **2019**, *2*, 362-370.

SDG Goals & Green Metrics

Millenium Development Goals: 8 focuses in 2000…..

https://www.unaa.org.au/2017/01/19/the-united-nations-millennium-development-goals-successes-and-failures-from-2000-until-today/

SDG Goals & Green Metrics

Sustainable Development Goals: 12 focuses on responsible and environmentally sustainable production and targets the substantial reduction of waste generation by 2030.

[THE 17 GOALS | Sustainable Development (un.org)](#)

SDG Goals & Green Metrics

Sustainable Development Goals: 12 focuses on responsible and environmentally sustainable production and targets the substantial reduction of waste generation by 2030.

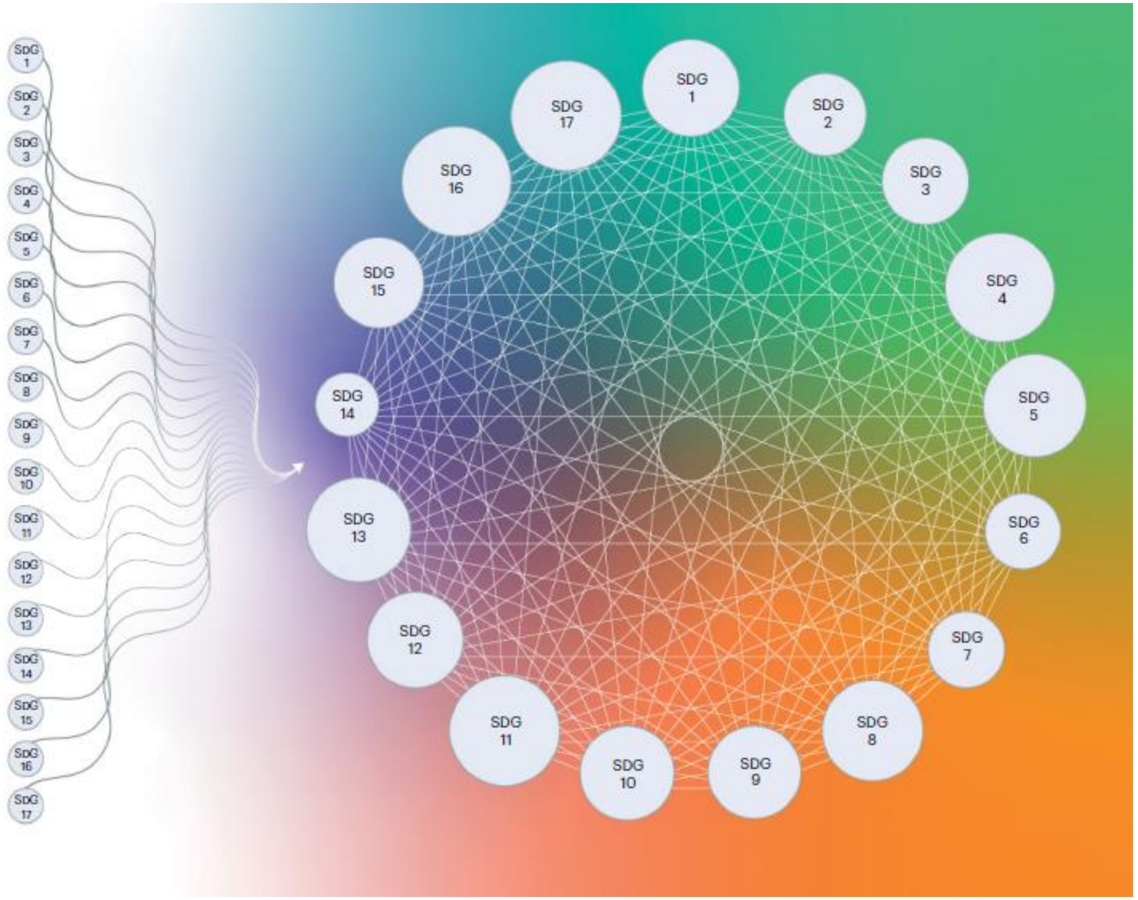
[THE 17 GOALS | Sustainable Development (un.org)]

Green Metrics: Real-Life Tools

Sustainable Development Goals: 12 focuses on responsible and environmentally sustainable production and targets the substantial reduction of waste generation by 2030.

For example:
Climate action (SDG13)
Make consumption and production more sustainable (SDG12)

Systemic impact means accounting for each goal's positive and negative influence on all other goals.



Weitz, N., Carlsen, H., Bennich, T. et al. Returning to core principles to advance the 2030 Agenda. Nat Sustain (2023). https://doi.org/10.1038/s41893-023-01212-7

Planetary Boundaries

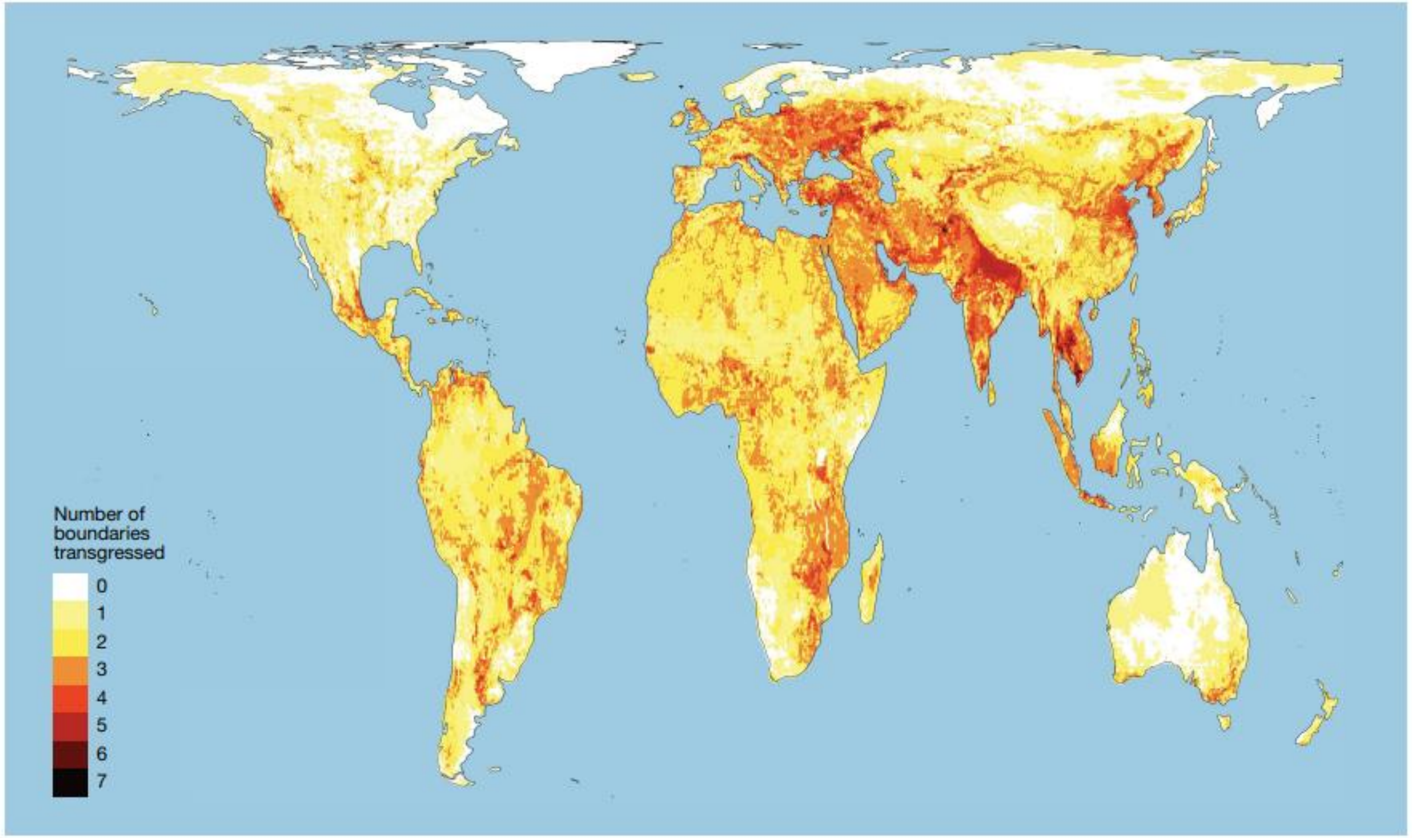


Fig. 3 | Hotspots of current ESB transgressions. The number of subglobal climate (two local exposure boundaries), functional integrity, surface water, groundwater, nitrogen, phosphorus and aerosol safe and just ESBs currently transgressed by location. No more than seven of these eight metrics have their ESBs transgressed in any one pixel. Since climate is a globally defined ESB, we use wet bulb temperatures of over 35 °C for at least 1 day per year and low-elevation coastal zones (<5 m) exposed to sea-level rise as proxies for local climate transgression while acknowledging that the impacts of climate change are far more diverse. We also emphasize that exposure of a location does not necessarily imply responsibility for causing or addressing these environmental impacts. We invite the reader to investigate the consequences of different boundary values using the code in the code availability information.

Rockström, J. *et al.*, Safe and just **E**arth **S**ystem **B**oundaries *Nature* **2023**, https://doi.org/10.1038/s41586-023-06083-8

Value of Nature

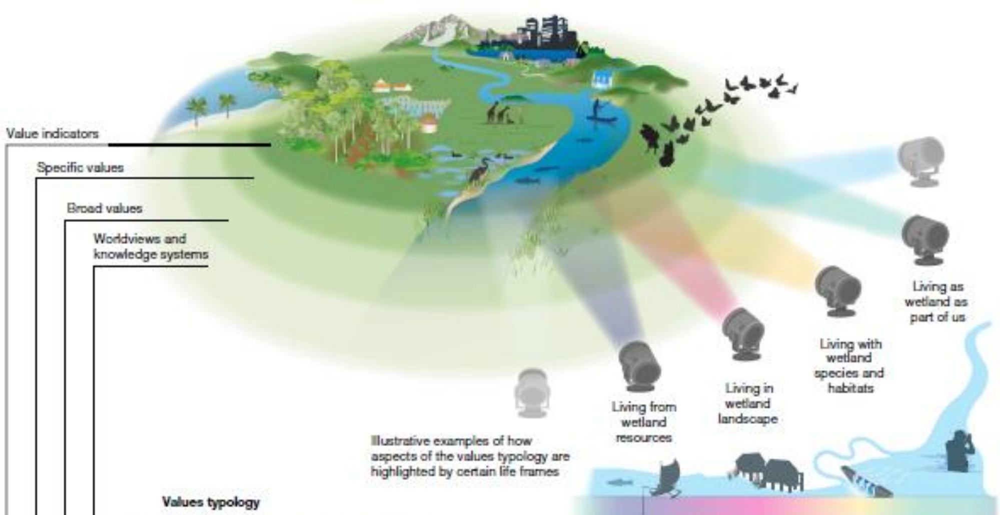
Plurality of values:

Postindustrial societies with high level of material security: increase in the value of wildlife

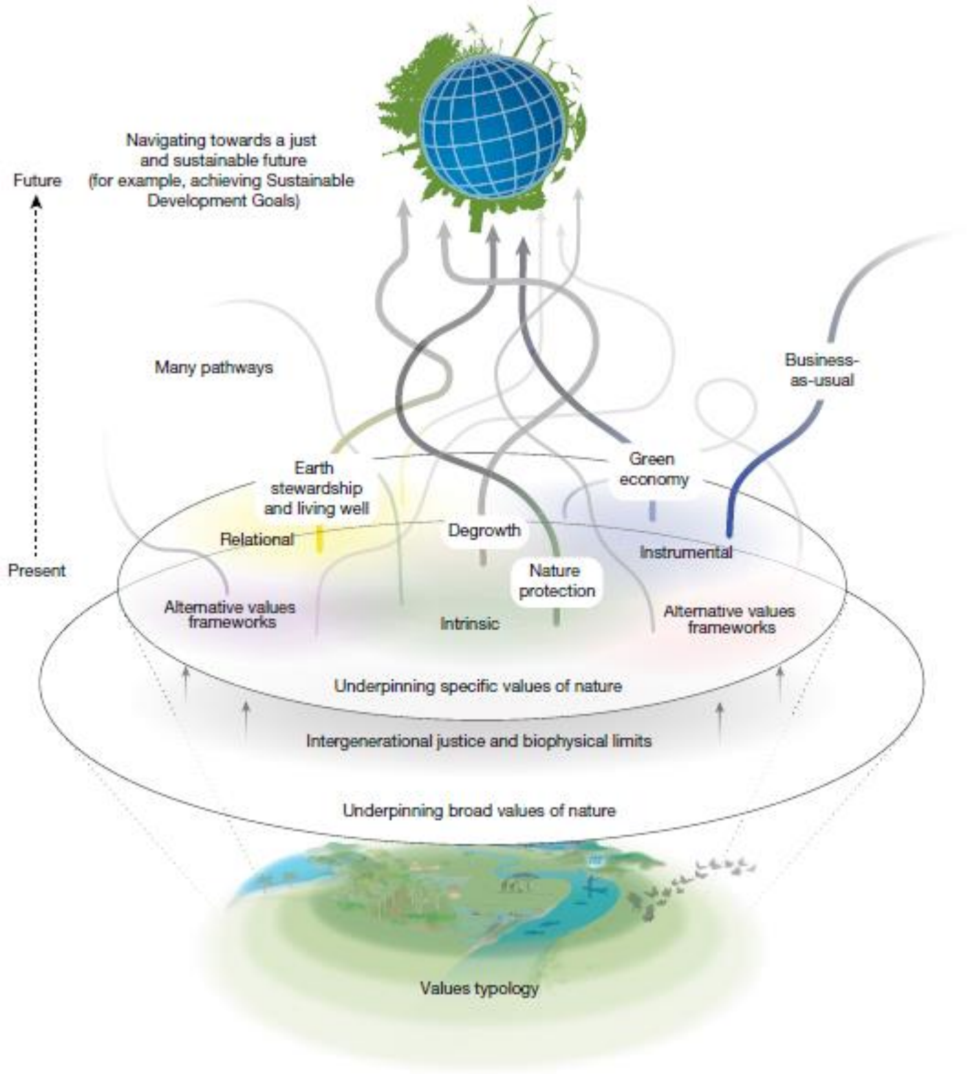
Global South: lower levels security; instrumental values…

Nature, **2023**, *620*, 821.
https://doi.org/10.1038/s41586-023-06406-9

Value of Nature

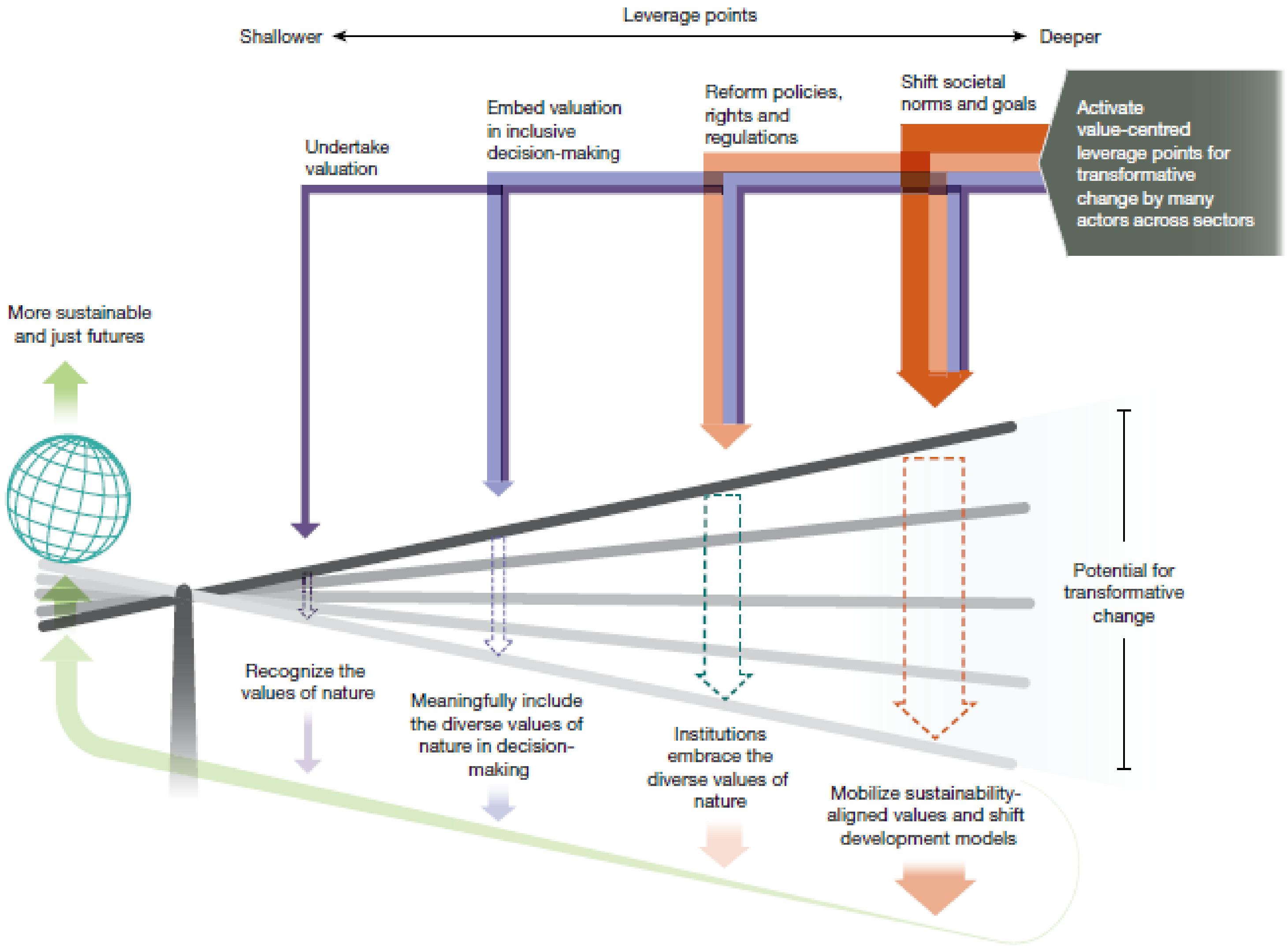


Values typology					
Worldviews	Ways through which people conceive and interact with the world	Anthropocentric	Anthropocentric	Bio/ecocentric	Pluricentric
Knowledge systems	Bodies of knowledge, practices and beliefs • Academic, indigenous, local				
Broad values	Guiding principles and life goals	Prosperity, livelihood	Belonging, health	Stewardship, responsibility	Oneness, harmony with nature
Specific values	Judgements regarding the importance of nature in particular situations				
	• Instrumental: means to an end, nature as a resource or asset, satisfaction of needs and preferences, usefulness for people	Fish to sell at market	Health benefits of recreation on the river	Fish as regulators of food web structure and function	Fish to eat
	• Intrinsic: agency of other-than-humans, inherent worth of biodiversity as ends in and of themselves			The right of fish to exist	Fish as co-inhabitants
	• Relational: importance of desirable, meaningful and often reciprocal human relationships	Cultural meanings of fishing	Sense of place of a fishing community	Awe inspired by spawning fish	Fish as part of kinship or clan relationships
Value indicators	Quantitative measures and qualitative descriptors				
	• Biophysical	Tonnes of fish	Physiological effects of being in nature	Number of fish species	Fish as nutrition
	• Monetary	Price premium of eco-certified fish	Willingness to pay (WTP) for recreational fishing	Non-use (that is, existence and bequest) WTP of a river feature	
	• Socio-cultural	Gender-specific participation in fishing	Ratings of special places	Legal standing of biodiversity	Narratives of sacred places



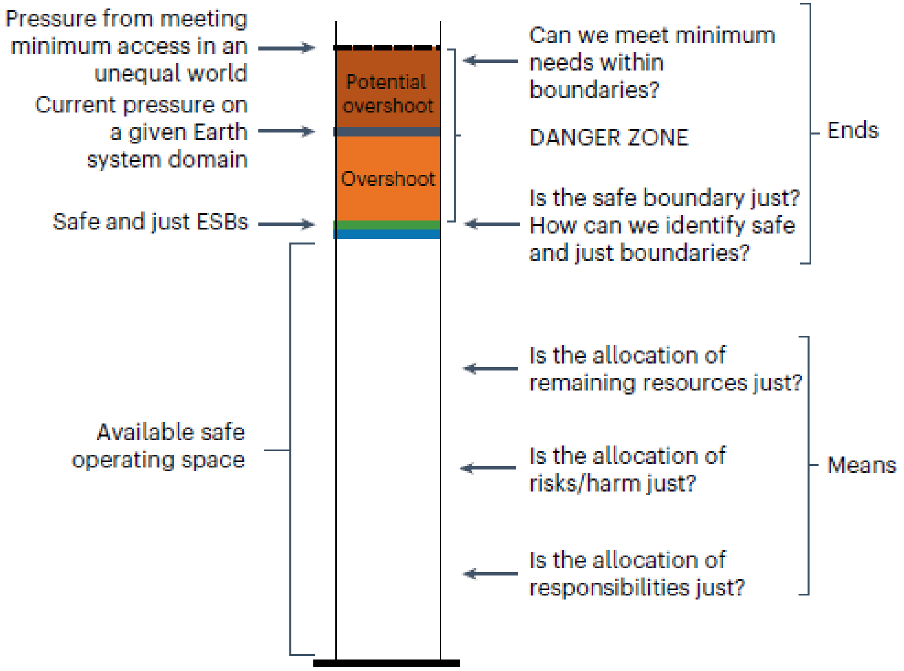
Nature, **2023**, *620*, 821.
https://doi.org/10.1038/s41586-023-06406-9

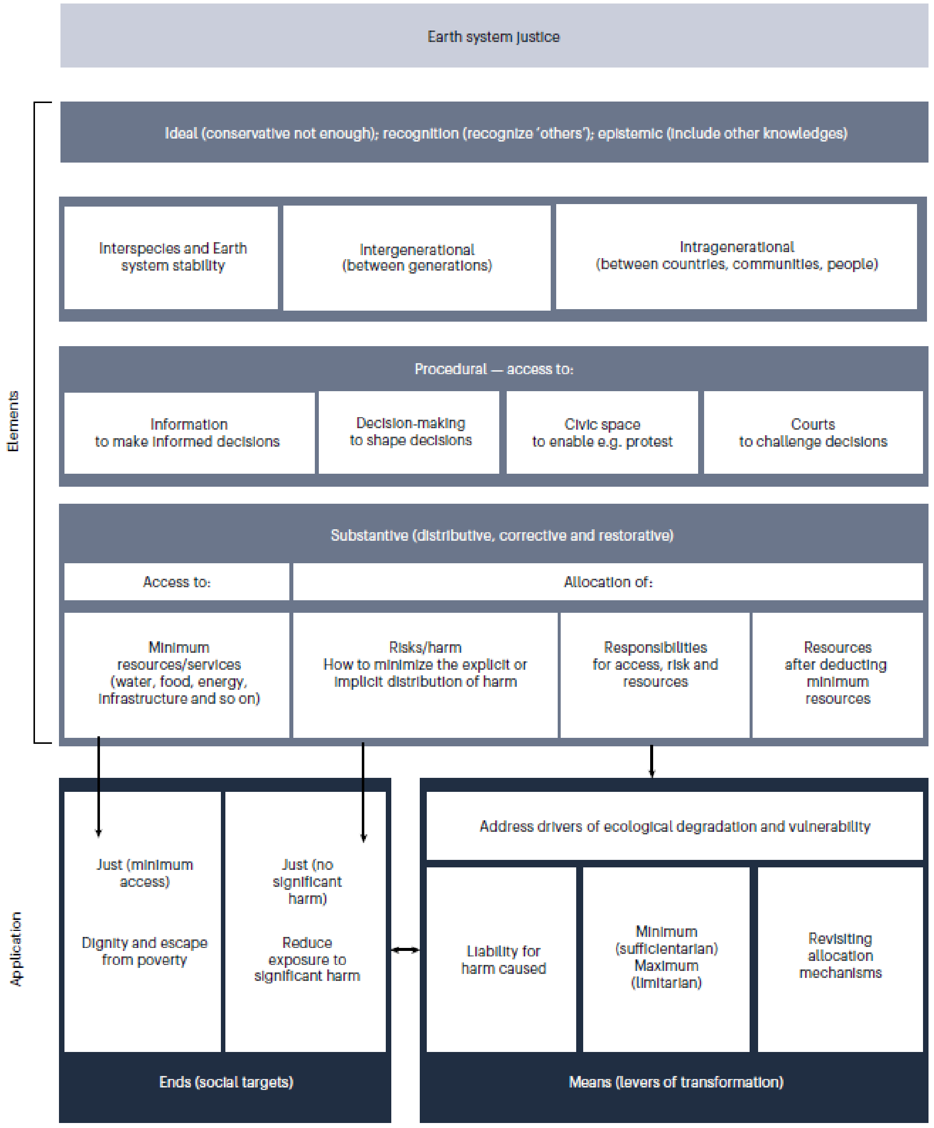
Value of Nature



Nature, **2023**, *620*, 821.
https://doi.org/10.1038/s41586-023-06406-9

Justice?





Nature Sustainability, **2023**
https://doi.org/10.1038/s41893-023-01064-1

Nature Sustainability, **2025,** Monetary impact valuation for sustainable business.
https://doi.org/10.1038/s41893-025-01630-9

Green Metrics: Real-Life Tools

"you can't manage what you don't measure"

Edwards Deming or Peter Drucker

«If you can't measure it, you can't improve it»

Lord Kelvin

"Nothing becomes more important just because you can measure it. It becomes more measurable, that's all"

Edwards Deming

Not everything that can be counted counts and not everything that counts can be counted

Einstein?

Green Chemistry Metrics by Frank Roschangar and Juan Colberg
in *Green Techniques for Organic Synthesis and Medicinal Chemistry*, Second Edition. Edited by Wei Zhang and Berkeley W. Cue.

Green Metrics: Real-Life Tools

Historical context:

Back in 1956, Nobel Price Winner Robert B. Woodward stated: “synthesis must always be carried out by a plan, and the synthetic frontier can be defined only in terms of the degree to which realistic planning is possible, utilizing all of the intellectual and physical tools available”

Woodward, R. B. (**1956**) *In Perspectives in Organic Chemistry* (ed. Todd, A.), 155–184.
Corey, E. J., Cheng, X.-M. (**1989**) *The Logic of Chemical Synthesis*. John Wiley & Sons, New York.
Green Chemistry Metrics by Frank Roschangar and Juan Colberg
in *Green Techniques for Organic Synthesis and Medicinal Chemistry*, Second Edition. Edited by Wei Zhang and Berkeley W. Cue. © 2018 John Wiley & Sons Ltd

Green Metrics: Real-Life Tools

Historical context:

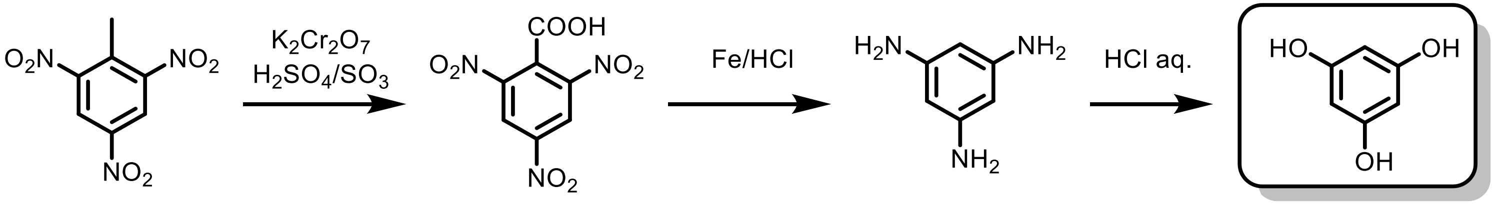
The ideal synthesis [...] may be defined as one in which the target molecule is prepared from readily available starting materials in one simple, safe, environmentally-acceptable, and resource-effective operation that proceeds quickly and in quantitative yield.”

Wender, P. A.; Miller, B. L. Organic Synthesis: Theory and Applications; Hudlicky, T., Ed.; JAI Press: Greenwich, CT, **1993**; Vol. 2, pp 27−66.

Green Metrics: Real-Life Tools

Historical context:

In 1980 for the production of Phloroglucinol: 200 MT/y the synthesis starts from TNT !!



$$C_7H_5N_3O_6 + K_2Cr_2O_7 + 5\ H_2SO_4 + 9\ Fe + 21\ HCl \longrightarrow C_6H_6O_3 + Cr_2(SO_4)_3 + 2\ KHSO_4 + 9\ FeCl_2 + 3\ NH_4Cl + CO_2 + 8\ H_2O$$

	$C_7H_5N_3O_6$	$K_2Cr_2O_7$	H_2SO_4	Fe	HCl	$C_6H_6O_3$	$Cr_2(SO_4)_3$	$KHSO_4$	$FeCl_2$	NH_4Cl	CO_2	H_2O
MW:	227	294	98	56	37	126	392	136	127	53	44	18

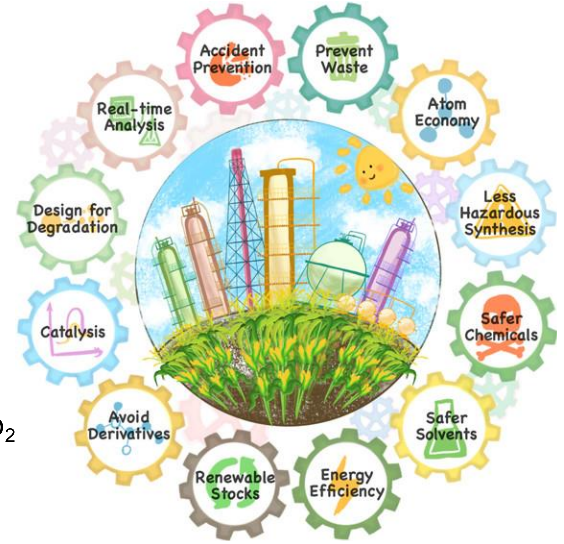
Atom Economy [AE]: 126/(126+392+2*136+9*127+3*53+44+8*18) = 5,5%

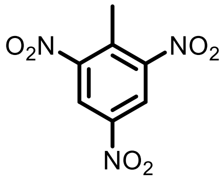
Sheldon, R. A. Metrics of Green Chemistry and Sustainability: Past, Present, and Future *ACS Sustainable Chem. Eng*. **2018**, *6*, 32-48

Green Metrics: Real-Life Tools

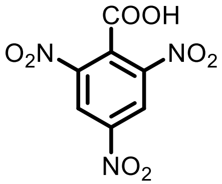
Historical context:

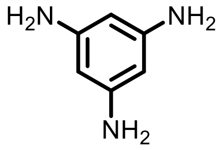
Production of Phloroglucinol: 200 MT/y





$K_2Cr_2O_7$
H_2SO_4/SO_3





Sheldon, R. A. Metrics of Green Chemistry and Sustainability: Past, Present, and Future *ACS Sustainable Chem. Eng*. **2018**, *6*, 32-48
Francisco Garca Calvo-Flores, Sustainable Chemistry Metrics *ChemSusChem* **2009**, *2*, 905.

Green Metrics: Real-Life Tools

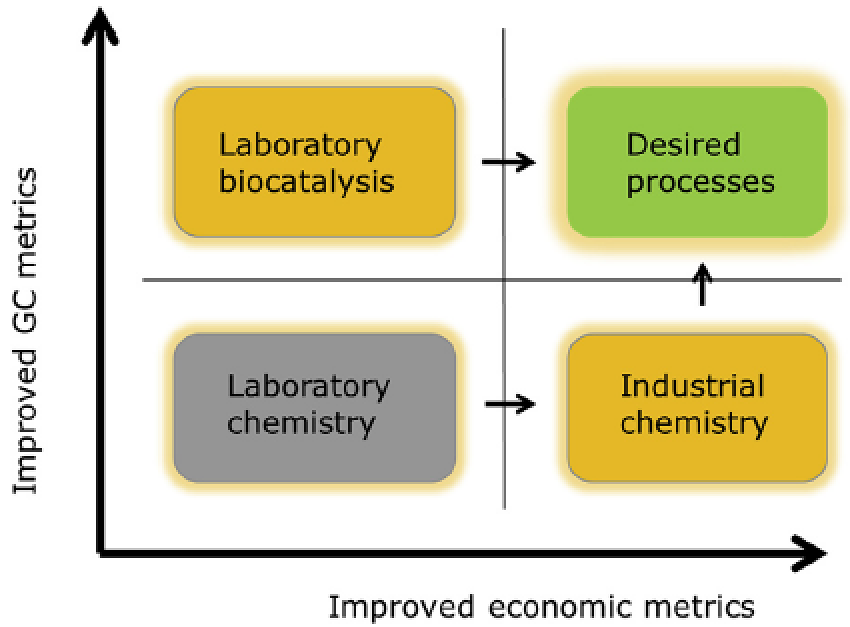
Can we measure the «greenness» of a Chemical Reaction or Process ?
How this could be done?

Can we compare 2 chemical steps or chemical processes and decide which one is «greener» ?

The accepted consensus for any metric is that it must be simple, easily measurable and clearly highlight the desired information

Monteith, E. R. *et al. Green Chem.* **2020**, *22*, 123.

Green Metrics: Real-Life Tools

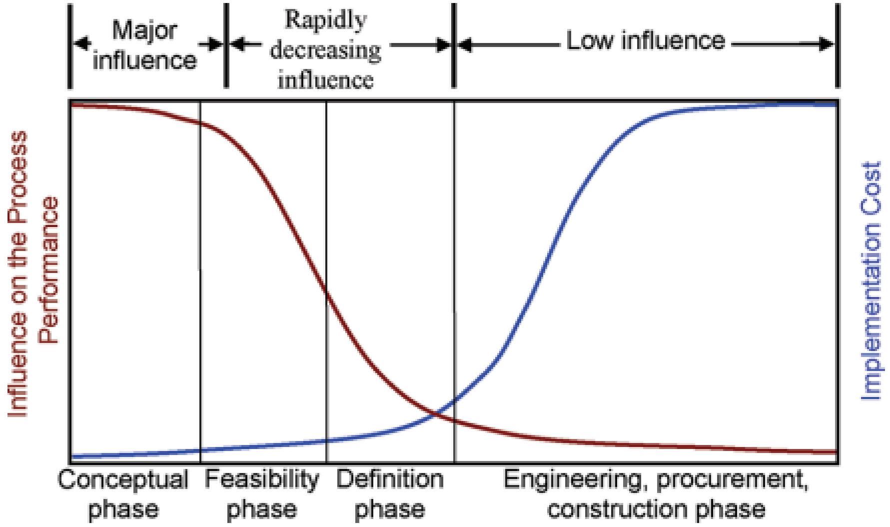


Contribution to environmental footprint and cost	Covered by existing metrics Y/N	Role of continuous manufacturing	Comment on cost contribution	Way to integrate contribution into environmental footprint and cost
Raw materials, solvents, water, catalysts	Y	Continuous manufacture may allow for cheaper raw materials, frequently disposal of waste streams is cheaper	Typically raw material cost is 20–50% of total manufacturing cost	Consider efficiency of use AND cost of raw material
Personnel cost for manufacturing	N	Required manpower may differ: more attention during start-up, less effort during stable operation	Need for specific training may add to start-up cost and create a hurdle. 10–30% cost contribution	Separate consideration of start-up and operation
Plant size, productivity, and idle time for reconfiguration	N	Important factors: higher productivity of generally smaller plant; reduces plant footprint; longer idle time lowers overall productivity	Calculate productivity and time demand for changeover and production. Calls for preconfiguration outside production hall. 10–30% contribution	Specific advantage if “minimally invasive” integration is possible
Asset depreciation vs consumables	N	Important factor. May be decisive for use of disposable components requiring less cleaning and thus lower material (solvent) input	Compare setup and removal of disposables to cleaning. 10–30% contribution	Treat certain plant components as consumables

Woodley, J. M. New frontiers in Biocatalysis for sustainable synthesis. *Curr. Opin. Green. Sustain. Chem*. **2020**, *21*, 22.

Green Metrics: Process Implementation

Material Flow Analysis



Ruiz-Mercado, G. J. *et al. Ind. Eng. Chem. Res.* **2012**, *51*, 2309-2328.

Green Metrics: Real-Life Tools

Historical context:

In 1991 Barry Trost defined:

The prime focal point in organic synthesis: Selectivity-chemo- (functional group differentiation), regio- (orientational control of two reacting partners), diastereo-(control of relative stereochemistry), and enantio- (control of absolute stereochemistry)

But **Atom Economy** defined as: how much of the reactants end up in the product has been overlooked!

$$AE = \frac{MW(Product) \times 100}{\sum MW(Raw\ Materials) + \sum MW(Reagents)}$$

Optimum Value= 100.

Trost, B. M. The atom economy–A search for synthetic efficiency. *Science*, **1991**, *254*, 1471–1477.
Sheldon, R. A. (**1992**) Organic synthesis: Past, present and future. Chem. Ind. (London), 23, 903-906.

Green Metrics: Real-Life Tools

Historical context:

In the 1992, Roger Sheldon defined the E-Factor

$$EFactor = \frac{\sum m(waste)}{m(Product)}$$

Optimum Value= 0.

$$EFactor = \frac{\sum m(Input\ Materials\ w.o.Water) - m\ (Product)}{m(Product)}$$

Sheldon, R. A. (**1992**) Organic synthesis: Past, present and future. Chem. Ind. (London), 23, 903-906.
Sheldon, R. A. Metrics of Green Chemistry and Sustainability: Past, Present, and Future ACS Sustainable Chem. Eng. **2018**, *6*, 32−48.

Green Metrics: Real-Life Tools

E Factor:

Industry Segment (Examples)	Annual Product Tonnage	E-Factor (kg waste/ kg product)	Total Annual Waste Tonnage	No. of Steps	Years of Development
Petrochemicals (Solvents, Detergents)	1,000,000–100,000,000	~0.1	10,000,000	"Separations"	100+
Bulk Chemicals (Plastics, Polymers)	10,000–1,000,000	<1–5	5,000,000	1–2	10–50
Fine Chemicals (Coatings, Electronic Parts, Pharmaceutical Raw Materials)	100–10,000	5–>50	500,000	3–4	4–7
Pharmaceuticals (Antibiotics, Drugs, Vaccines)	10–1,000	25–>100	100,000	6+	3–5

Roschangar, F.; Colberg, J. (**2018**) Green Chemistry Metrics in Green Techniques for Organic Synthesis and Medicinal Chemistry, Second Edition. Wiley.

Green Metrics: Real-Life Tools

Historical context:

AE and E-Factor, pros vs cons:

AE assumed a chemical yield of 100% whereas E-Factor took it into account
AE does not considered selectivity of the reaction
E-Factor did not take into account water used
E-Factor considered all waste the same….1 kg NaCl vs 1kg of CrO_3

AE is easily applied to a one-step reaction whereas E-Factor allows a holistic assessment of a complete Process.
AE allows a rapid evaluation of waste between 2 processes.
E-Factor: What is a waste?
Acid gas scrubbing, pH adjustment in waste treatment plants, etc. included?
Is waste that is produced as a result of energy use (heating or cooling reactions, abatement technology, etc)
Is waste solvent passed on to a waste handler to be burned in a cement kiln included?

Both do not take into account: chemical toxicity, safety risks, energy consumption, etc.

Sheldon, R. *Green Chem.*, **2007**, *9*, 1273.
Sheldon, R. *Green Chem.*, **2017**, *19*, 18.

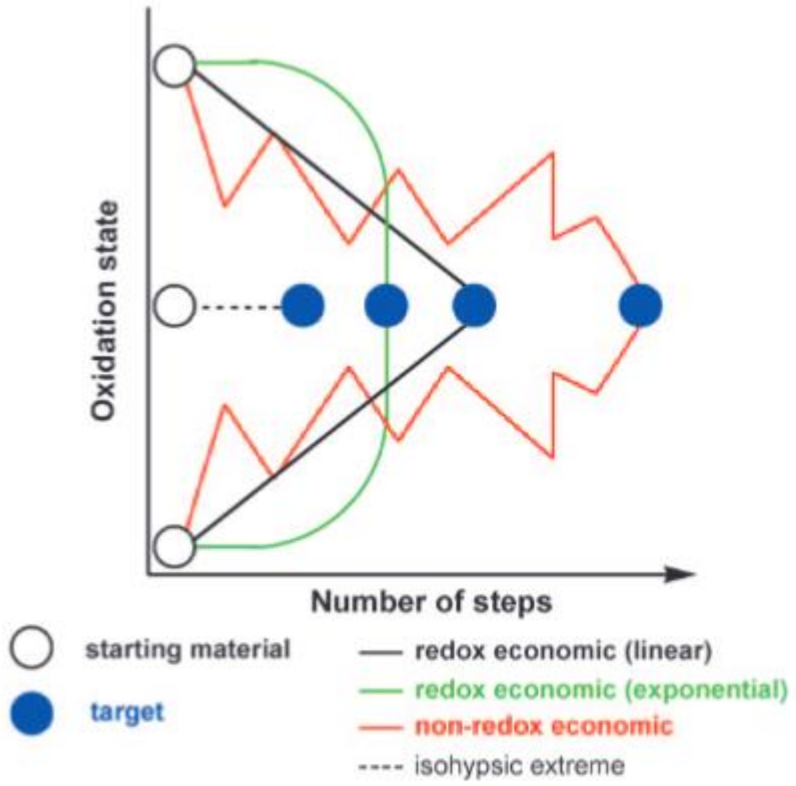
Constanble, D. J. C. *et al. Green Chem.* **2002**, *4*, 521.

Green Metrics: Real-Life Tools

Ideality & Complexity:

$$\%\text{ideality} = \frac{[(\text{no. of construction rxns}) + (\text{no. of strategic redox rxns})]}{(\text{total no. of steps})} \times 100$$

Complexity = %ideality × total no. of reaction
Complexity = no. of construction reactions + no. of strategic redox reactions



Burns, N. Z.; Baran, P. S.; Hoffmann, R. W. Redox Economy in Organic Synthesis *Angew. Chem. Int. Ed.* **2009**, *48, 2854.*
Gaich, T.; Baran, P. S. Aiming for the Ideal Synthesis *J. Org. Chem.* **2010**, 75, 4657.
Roschangar, F.; Sheldon, R. A.; Senanayake, C. H. *Green Chem.*, **2015**, *17*, 752.

Green Metrics: Real-Life Tools

Development of New Metrics: Pharma industries

Need for others metrics

Reaction **M**ass **E**fficiency
included all reactant mass, yield & atom economy

$$\mathrm{RME} = \frac{m(Product) \times 100}{\sum m(Raw\ Materials)}$$

Optimum Value= 100.

But: does not include all the other materials: reagents, solvents, catalysts.

Curzons, A. D. *et al. Green Chem.* **2001**, *3*, 1.
Constanble, D. J. C. *et al. Green Chem.* **2002**, *4*, 521.

Green Metrics: Real-Life Tools

Development of New Metrics: Pharma industries

Mass **I**ntensity & **P**rocess **M**ass **I**ntensity:

$$\mathrm{MI} = \frac{Total\ mass\ used\ in\ a\ process\ step\ or\ a\ process\ (kg)(excl.water)}{Mass\ of\ Product\ (kg)}$$

Optimum Value= 1.

$$\mathrm{PMI} = \frac{Total\ mass\ used\ in\ a\ process\ step\ or\ a\ process\ (kg)(incl.water)}{Mass\ of\ Product\ (kg)}$$

Optimum Value= 1.

Curzons, A. D. *et al. Green Chem.* **2001**, *3*, 1.
Constanble, D. J. C. *et al. Green Chem.* **2002**, *4*, 521.
Jimenez-Gonzalez, C. et al. *Org. Process Res. Dev.* **2011**, *15*, 912,

Green Metrics: Real-Life Tools

Development of New Metrics: Pharma industries

Process **M**ass **I**ntensity:

$$\mathrm{PMI} = \frac{Total\ mass\ used\ in\ a\ process\ step\ or\ a\ process\ (kg)(incl.water)}{Mass\ of\ Product\ (kg)}$$

Optimum Value= 1.

Good indicator of the efficiency of a step or a synthesis

Curzons, A. D. *et al. Green Chem.* **2001**, *3*, 1.
Constanble, D. J. C. *et al. Green Chem.* **2002**, *4*, 521.
Jimenez-Gonzalez, C. et al. *Org. Process Res. Dev.* **2011**, *15*, 912,

Green Metrics: Real-Life Tools

Development of New Metrics: Pharma industries

PMI vs *cEFactor*

$$cEFactor = \frac{\sum m(Input\ Materials\ incl.Water) - m\ (Product)}{m(Product)}$$

$cEFactor$ = PMI - 1

There is more than «-1» !

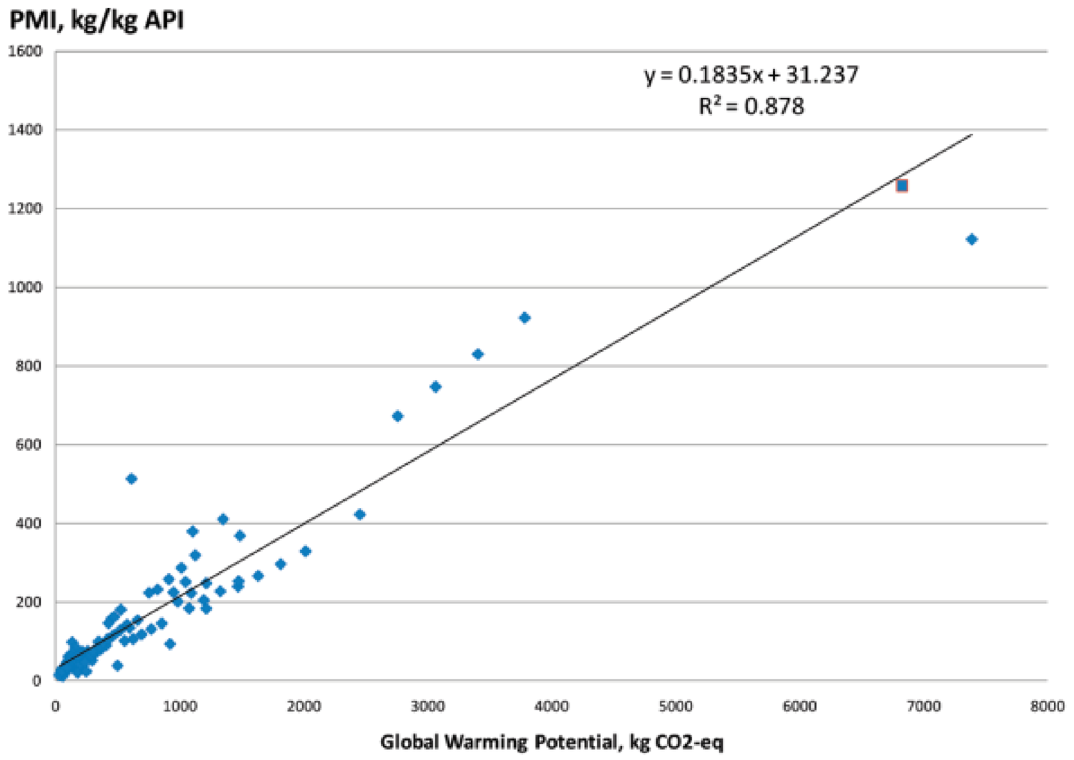
“end-of-pipe view of waste-management philosophy from the 1980s”

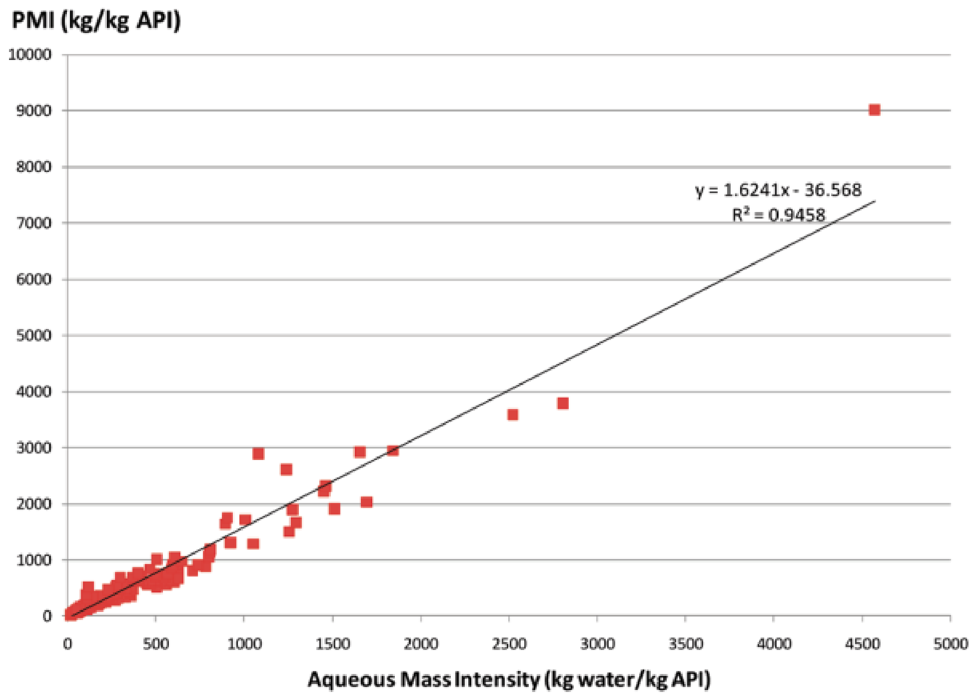
Jimenez-Gonzalez, C. et al. *Org. Process Res. Dev.* **2011**, *15*, 912.

Green Metrics: Real-Life Tools

PMI vs *cEFactor*

"Simply put, the good focus is on minimizing waste. The greater focus is on maximizing value and efficiency. If one maximizes value, waste reduction will be one of the benefits."





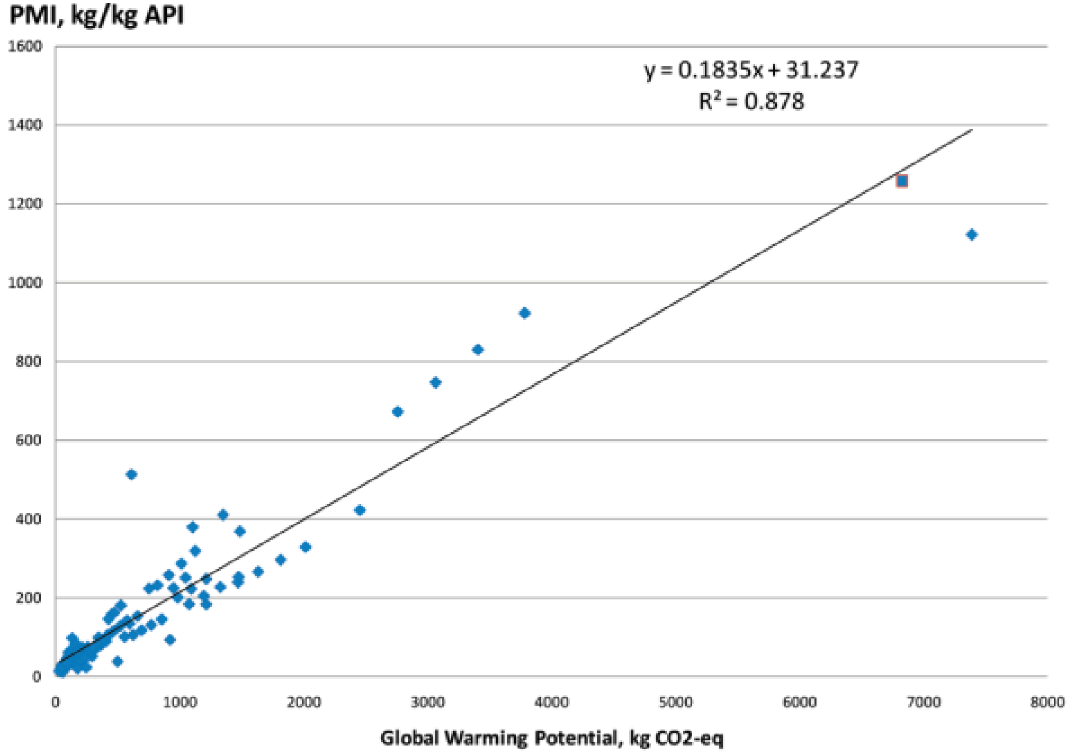
all development compounds in GlaxoSmithKline's portfolio (2011)

Jimenez-Gonzalez, C. et al. *Org. Process Res. Dev.* **2011**, *15*, 912.

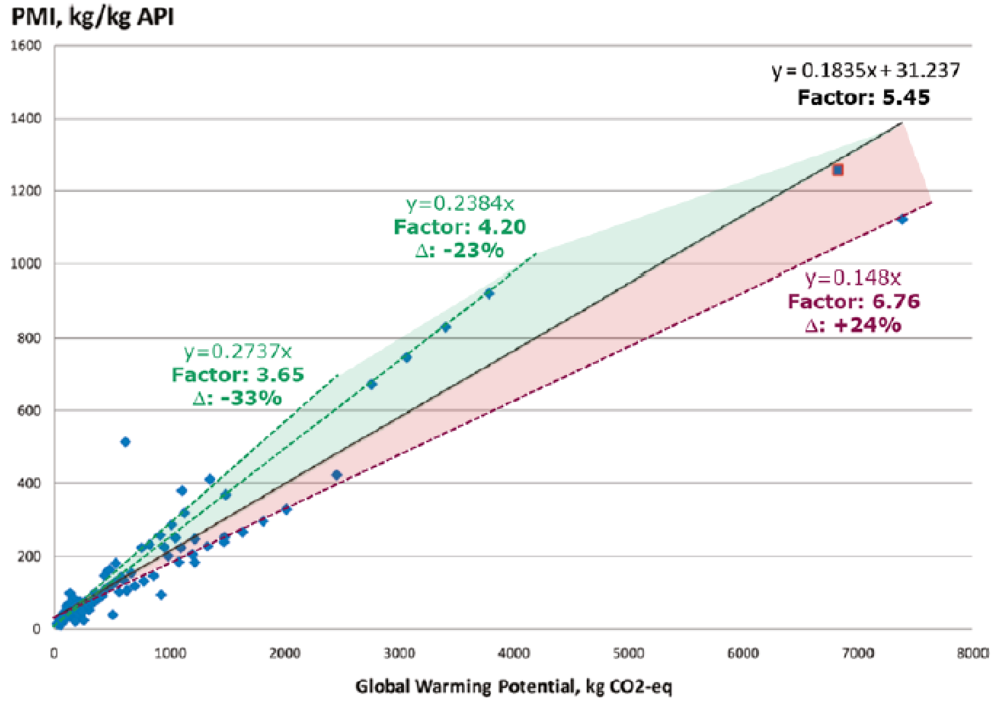
Green Metrics: Real-Life Tools

PMI vs *cEFactor*

"Simply put, the good focus is on minimizing waste. The greater focus is on maximizing value and efficiency. If one maximizes value, waste reduction will be one of the benefits."



all development compounds in GlaxoSmithKline's portfolio (2011)



Colorful visualization of deviation from average PMI GWP correlation was performed at Merck KGA , Darmstadt, Germany for benchmarking

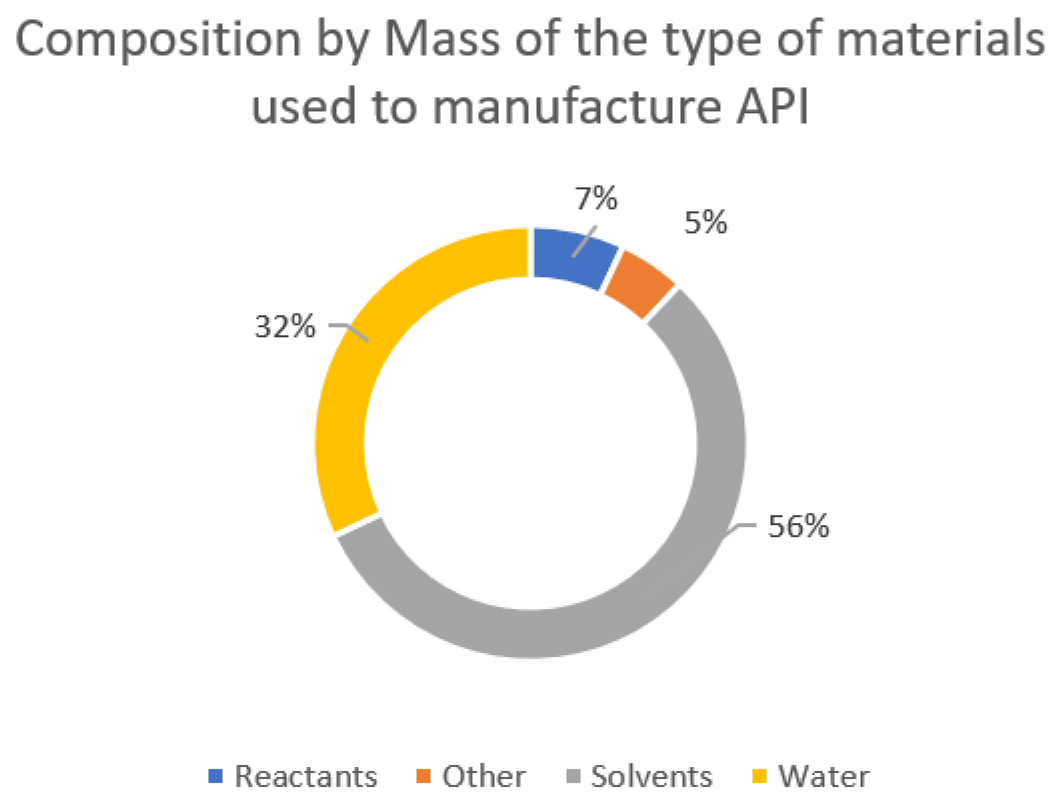
Internal Presentation.

Jimenez-Gonzalez, C. et al. *Org. Process Res. Dev.* **2011**, *15*, 912.

Green Metrics: Real-Life Tools

PMI

ACS GCI Pharmaceutical Roundtable 2008



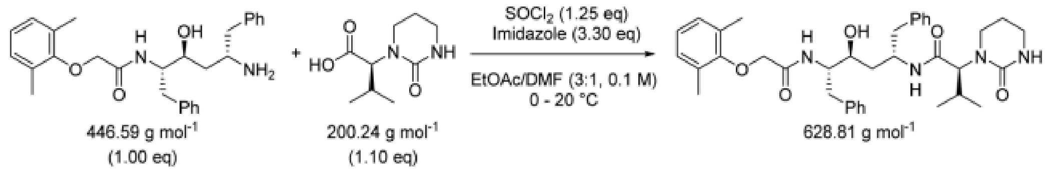
Biggest waste contributor

Jimenez-Gonzalez, C. et al. *Org. Process Res. Dev.* **2011**, *15*, 912.
Monteith, E. R. *et al. Green Chem.* **2020**, *22*, 123.

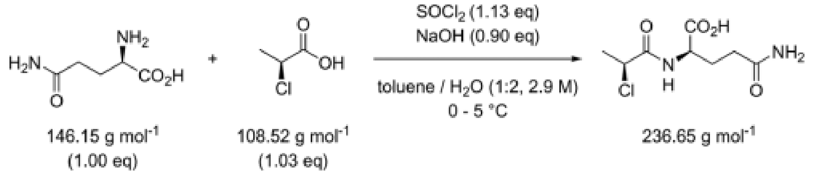
PMI

PMI Potential Pitfalls

Reaction 1



Reaction 2

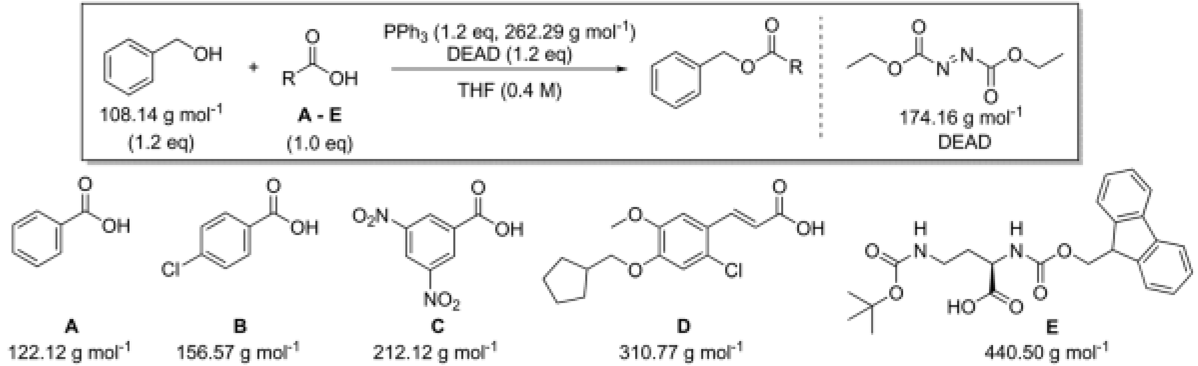


	AE (%)	RME (%)	PMI (g g^{-1})	PMI_{RRC} (g g^{-1})	PMI_{Solv} (g g^{-1})	Yield (%)
Literature data reported						
Reaction 1: [Acid] = 0.1 M	97	87	17.3	1.8	15.5	92
Reaction 2: [Acid] = 2.9 M	93	75	3.9	2.2	1.7	81
Simulation A: [Acid] = 0.4 M, literature yield						
Reaction 1	97	87	5.7	1.8	3.9	92
Reaction 2	93	75	14.6	2.2	12.4	81
Simulation B: [Acid] = literature data, yield = 90%						
Reaction 1	97	85	17.7	1.8	15.8	90
Reaction 2	93	83	3.5	2.0	1.5	90
Simulation C: [Acid] = 0.4 M, yield = 90%						
Reaction 1	97	85	5.8	1.8	4.0	90
Reaction 2	93	83	13.2	2.0	11.2	90
Simulation D: [Acid] = 0.4 M, yield = 50%						
Reaction 1	97	47	10.5	3.3	7.2	50
Reaction 2	93	46	23.7	3.5	20.2	50

Monteith, E. R. *et al. Green Chem.* **2020**, *22*, 123.

PMI

PMI Potential Pitfalls



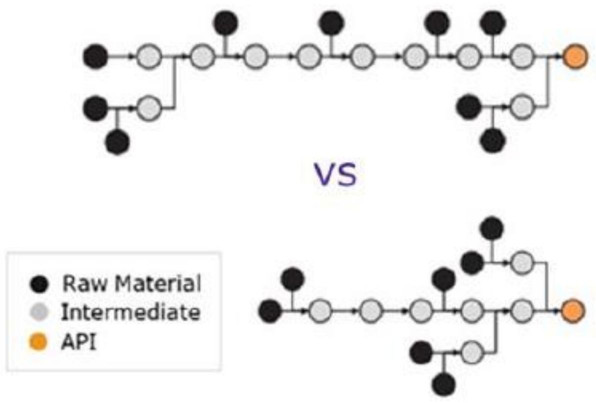
Carboxylic acid	AE (%)	RME (%)	PMI ($g\ g^{-1}$)	PMI_{RRC} ($g\ g^{-1}$)	PMI_{Solv} ($g\ g^{-1}$)	Yield (%)
Simulation 1: [Acid] = 0.4 M, yield = 90%						
A	92	76	15.7	4.1	11.6	90
B	93	78	13.7	3.6	10.0	90
C	94	80	11.4	3.2	8.2	90
D	96	82	8.8	2.7	6.2	90
E	97	84	6.9	2.3	4.7	90
Simulation 2: [Acid] = 0.4 M, yield = 80%						
A	92	67	17.7	4.6	13.1	80
B	93	69	15.4	4.1	11.3	80
C	94	71	12.8	3.6	9.2	80
D	96	73	9.9	3.0	6.9	80
E	97	74	7.8	2.6	5.2	80
Simulation 3: [Acid] = 0.4 M, yield = 70%						
A	92	59	20.2	5.2	15.0	70
B	93	60	17.6	4.7	12.9	70
C	94	62	14.6	4.1	10.5	70
D	96	64	11.4	3.4	7.9	70
E	97	65	8.9	2.9	6.0	70

Monteith, E. R. *et al. Green Chem.* **2020**, *22*, 123.

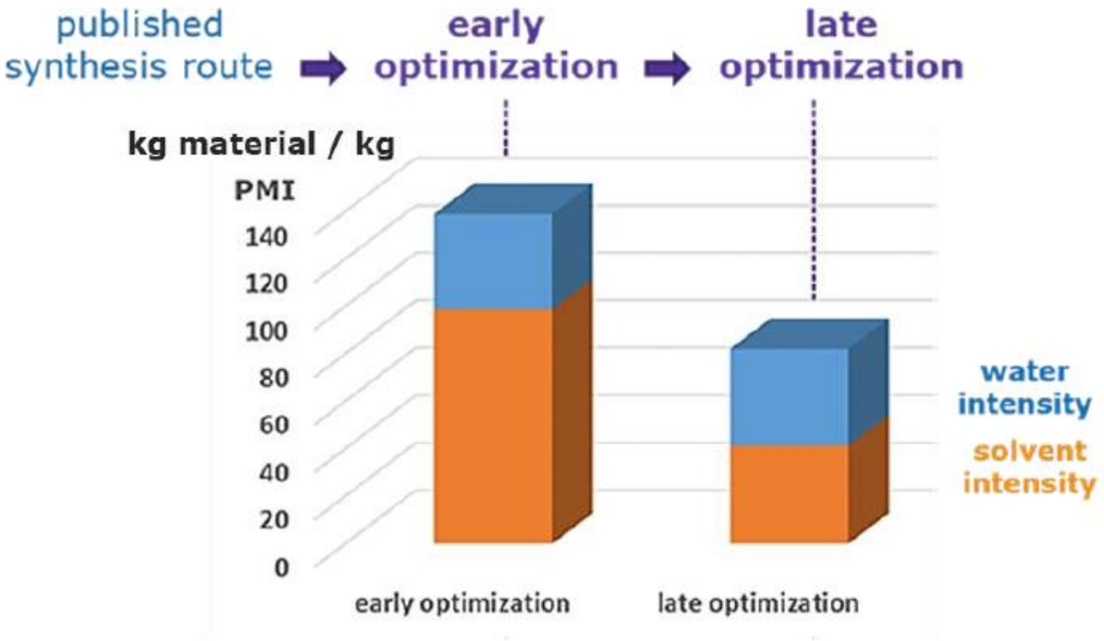
PMI

PMI: comparison of different routes & selection tool

How to compare 2 routes:
Metrics could help!



After selection: Optimization!



Safety and Hazard Metrics

Thermal Hazard
Reagent Hazard
Pressure
Hazardous by-product
Waste: metal, toxicity, upcycling

Solvent Usage: number, recovery
Mass Intensity of Solvent

Biodegradation, Bioaccumulation, Energy use

Curzons, A. D.; Constable, D. J. C.; Mortimera, D. N.; Cunningham, V. L. So you think your process is green, how do you know?—Using principles of sustainability to determine what is green–a corporate perspective *Green Chem.*, **2001**, *3*, 1–6.

Specificity of Perfumery Ingredients

Natural oil extraction
Biotechnology Processes

Metrics should be easy to understand by our clients and final consumers

Our competitors are also our clients: Needs for metrics that could be asked or guessed with the highest accuracy possible

Green Metrics: Real-Life Tools

Solvents, Water:

Solvent **I**ntensity: $$SI = \frac{\sum m(Solvents\ excl.Water)}{m(Product)}$$ Optimum Value= 0.

Water **I**ntensity: $$WI = \frac{\sum m(Water)}{m(Product)}$$ Optimum Value= 0.

Curzons, A. D. *et al. Green Chem.* **2001**, *3*, 1.
Jimenez-Gonzalez, C. *et al. Clean Prod. Processes* **3**, 35.

Solvents Guide

Solvent:

Required during a reaction:

- enable heat transfer
- mass transfer

Required during post-reaction processing and isolation of products

No solvent could be the ideal choice…

…but could participate in increasing the safety of chemical reactions

And also cleaning of the installations

For a recent perspective in the Crop Protection Industry: Dutta, P. *et al. Green Chem.* **2022**, *24*, 3943.

Solvents Guide

GSK's guide

Solvent	Health	Safety	Env.	EHS flag	Sum[a]
Water	10	10	4	0	24
MeOH	5	5	4	0	14
EtOH	8	6	3	0	17
i-PrOH	8	6	3	0	17
n-BuOH	5	8	5	0	18
t-BuOH	6	6	3	0	15
Benzyl alcohol	7	7	6	0	20
Ethylene glycol	7	9	5	0	21
Acetone	8	4	3	0	15
MEK	8	4	3	0	15
MIBK	6	7	2	0	15
Cyclohexanone	6	8	6	0	20
Methyl acetate	7	4	3	0	14
Ethyl acetate	8	4	4	0	16
i-PrOAc	7	6	5	0	18
n-BuOAc	8	8	5	0	21
Diethyl ether	5	2	4	−8	3
DIPE	8	1	3	−8	4
MTBE	5	3	4	−8	4
THF	6	3	3	−8	4
Me-THF	4	3	4	0	11
1,4-Dioxane	4	4	3	0	11
Anisole	7	6	5	0	18
DME	2	4	4	−8	2
Pentane	8	2	5	−8	7
Hexane	4	2	3	−8	1
Heptane	8	3	3	0	14
Cyclohexane	7	2	5	0	14
Me-cyclohexane	8	3	5	0	16
Benzene	1	3	5	−8	1
Toluene	4	4	3	0	11
Xylenes	6	5	2	0	13
DCM	4	6	3	−8	5
Chloroform	3	6	3	−8	4
CCl_4	3	4	4	−8	3
DCE	2	6	4	−8	4
Chlorobenzene	4	8	6	0	18
Acetonitrile	6	6	2	0	14
DMF	2	9	4	−8	7
DMAc	2	8	2	−8	4
NMP	3	8	4	−8	7
DMPU	4	7	3	0	14
DMSO	7	2	5	0	14
Sulfolane	6	10	5	0	21
Nitromethane	4	2	3	−8	1
Methoxy-ethanol	2	6	3	−8	3
Acetic acid	6	7	4	0	17
Ac_2O	4	6	5	0	15
Pyridine	4	7	2	−8	5
TEA	3	4	4	−8	3

Astra-Zeneca's guide

Solvent	Health	Safety	Envir.	Sum[a]
MeOH	5	7	7	19
EtOH	2	7	7	16
i-PrOH	3	7	6	16
n-BuOH	4	7	6	17
t-BuOH	6	7	7	20
Acetone	6	7	8	21
MEK	7	7	7	21
MIBK	6	7	9	22
Ethyl acetate	5	7	6	18
i-PrOAc	4	7	7	18
n-BuOAc	2	7	4	13
Diethyl ether	7	10	10	27
MTBE	9	7	8	24
THF	8	7	8	23
Me-THF	8	7	9	24
1,4-Dioxane	9	10	9	28
Anisole	2	10	6	18
DME	10	3	8	21
Hexane	6	10	10	26
Heptane	3	10	8	21
Cyclohexane	6	10	9	25
Toluene	5	10	7	22
Xylenes	2	10	7	19
DCM	9	1	10	20
Chlorobenzene	9	7	9	25
Acetonitrile	8	7	9	24
DMF	9	3	8	20
DMAc	9	3	8	20
NMP	9	1	8	18
DMSO	1	1	6	8
Sulfolane	1	1	7	9
Methoxy-ethanol	10	3	8	21
Formic acid	10	3	7	20
Acetic acid	8	3	6	17
Pyridine	9	7	10	26
TEA	10	7	3	23

Henderson. R. K. *et al. Green Chem.* **2011**, *13*, 854.
Winterton, N. *Clean Technologies and Environmental Policy* **2021**, *23*, 2499.

Solvents Guide

Solvents Guides:

Family	Solvent	AZ	GCI-PR	GSK	Pfizer	Sanofi[a]	Issues	Overall[b]
Water	Water	—	—	24	Preferred	Recommended	—	Recommended
Alcohols	MeOH	19	14	14	Preferred	Recommended	—	TBC
	EtOH	16	13	17	Preferred	Recommended	—	Recommended
	i-PrOH	16	16	17	Preferred	Recommended	—	Recommended
	n-BuOH	17	13	18	Preferred	Recommended	—	Recommended
	t-BuOH	20	15	15	Preferred	Subst. adv.	—	TBC
	Benzyl alcohol	—	11	20	—	Subst. adv.	—	TBC
	Ethylene glycol	—	13	21	Usable	Subst. adv.	—	TBC
Ketones	Acetone	21	15	15	Preferred	Recommended	—	TBC
	MEK	21	16	15	Preferred	Recommended	—	TBC
	MIBK	22	17	15	—	Recommended	—	TBC
	Cyclohexanone	—	14	20	—	Subst. adv.	—	TBC
Esters	Methyl acetate	—	14	14	—	Subst. adv.	—	TBC
	Ethyl acetate	18	15	16	Preferred	Recommended	—	Recommended
	i-PrOAc	18	13	18	Preferred	Recommended	—	Recommended
	n-BuOAc	13	14	21	—	Recommended	—	Recommended
Ethers	Diethyl ether	27	21	3	Undesirable	Banned	H224	HH
	Diisopropyl ether	—	—	4	Undesirable	Subst. adv.	Perox.	Hazardous
	MTBE	24	21	4	Usable	Subst. adv.	—	TBC
	THF	23	16	4	Usable	Subst. adv.	H351	TBC
	Me-THF	24	15	11	Usable	Recommended	—	Problematic
	1,4-Dioxane	28	21	11	Undesirable	Subst. req.	—	Hazardous
	Anisole	18	13	18	—	Recommended	—	Recommended
	DME	21	23	2	Undesirable	Subst. req.	H360	Hazardous
Hydrocarbons	Pentane	—	—	7	Undesirable	Banned	H224	Hazardous
	Hexane	26	21	1	Undesirable	Subst. req.	—	Hazardous
	Heptane	21	17	14	Usable	Subst. adv.	—	Problematic
	Cyclohexane	25	18	14	Usable	Subst. adv.	—	TBC
	Me-cyclohexane	—	17	16	Usable	Subst. adv.	—	Problematic
	Benzene	—	21	1	Undesirable	Banned	H350	HH
	Toluene	22	18	11	Usable	Subst. adv.	H351	Problematic
	Xylenes	19	15	13	Usable	Subst. adv.	—	Problematic
Halogenated	DCM	20	18	5	Undesirable	Subst. adv.	H351	TBC
	Chloroform	—	18	4	Undesirable	Banned	—	HH
	CCl_4	—	19	3	Undesirable	Banned	H420	HH
	DCE	—	19	4	Undesirable	Banned	H350	HH
	Chlorobenzene	25	16	18	—	Subst. adv.	—	Problematic
Aprotic polar	Acetonitrile	24	14	14	Usable	Recommended	—	Problematic
	DMF	20	17	7	Undesirable	Subst. req.	H360	Hazardous
	DMAc	20	16	4	Undesirable	Subst. req.	H360	Hazardous
	NMP	18	16	7	Undesirable	Subst. req.	H360	Hazardous
	DMPU	—	—	14	—	Subst. adv.	—	Problematic
	DMSO	8	15	14	Usable	Subst. adv.	—	Problematic
	Sulfolane	9	13	21	—	Subst. adv.	—	Recommended
	Nitromethane	—	—	1	—	Banned	Explo.	HH
Miscellaneous	Methoxy-ethanol	21	20	3	—	Subst. req.	H360	Hazardous
Acids	Formic acid	20	15	—	—	Subst. req.	—	TBC
	Acetic acid	17	15	17	Usable	Subst. adv.	—	TBC
	Ac_2O	—	16	15	—	Subst. adv.	—	TBC
Amines	Pyridine	26	16	5	Undesirable	Subst. adv.	—	TBC
	TEA	23	18	3	—	Subst. req.	—	Hazardous

[a] Subst. adv.: substitution advisable; Subst. req.: substitution requested. [b] TBC: to be confirmed; HH: highly hazardous.

Prat, D. *et al. Green Chem.* **2014**, *16*, 4546.
Winterton, N. *Clean Technologies and Environmental Policy* **2021**, *23*, 2499.

Solvents Guide

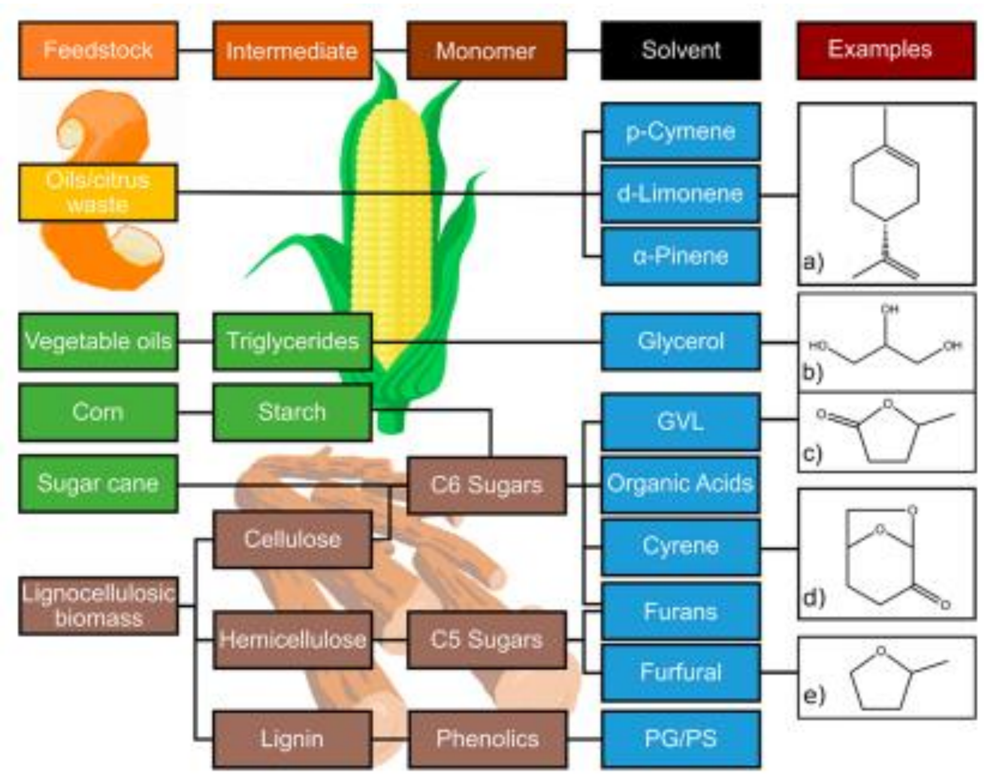
Solvents Guide:

Recommended	Water, EtOH, i-PrOH, *n*-BuOH, EtOAc, i-PrOAc, *n*-BuOAc, anisole, sulfolane.
Recommended or problematic?	MeOH, *t*-BuOH, benzyl alcohol, ethylene glycol, acetone, MEK, MIBK, cyclohexanone, MeOAc, AcOH, Ac_2O.
Problematic	Me-THF, heptane, Me-cyclohexane, toluene, xylenes, chlorobenzene, acetonitrile, DMPU, DMSO.
Problematic or hazardous?	MTBE, THF, cyclohexane, DCM, formicacid, pyridine.
Hazardous	Diisopropyl ether, 1,4-dioxane, DME, pentane, hexane, DMF, DMAc, NMP, methoxy-ethanol, TEA.
Highly hazardous	Diethyl ether, benzene, chloroform, CCl_4, DCE, nitromethane.

Solvent selection based on a conceptual process design by combining cost evaluation and life cycle assessments for developing new reaction pathways: T. Yamaki *et al. Green Chem.*, **2024**, *26*, 3758.

Solvents Guide

Solvents Biosourced:



Coby J. Clarke *et al.* Green and Sustainable Solvents in Chemical Processes *Chem. Rev*. **2018**, *118*, 747-800.
Alonso, D. M. *et al. Green Chem.* **2013**, *15*, 584.

Solvents Guide

Solvent recycling:

Key properties affecting recyclability:

- Boiling point (i.e., ease of distillation)
- Number of solvents with a boiling point within 10°C (influencing ease of solvent separability)
- Number of azeotropes with other solvents
- Relative ease of drying (most solvents are needed dry)
- Risk on recovery (e.g., via peroxide formation)
- Reactivity (e.g., esters may hydrolyze)
- Water solubility (affecting the potential loss in aqueous streams) Issues

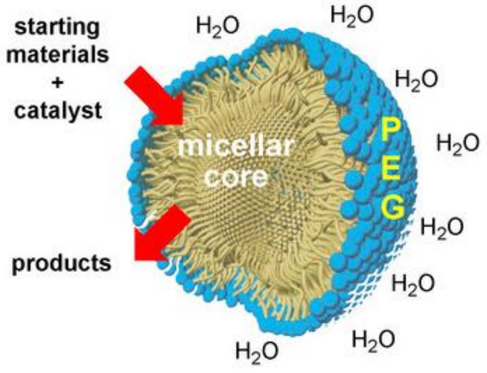
But risk of contamination !

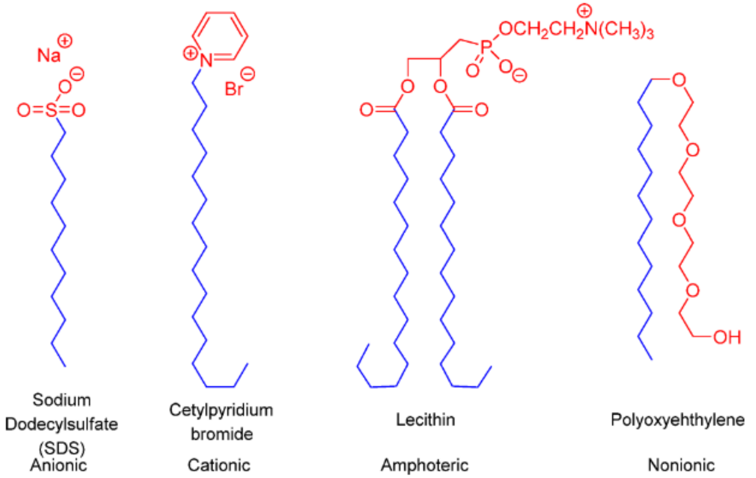
Curzons, A. D. *et al. Clean Products and Processes* **1999**, *1*, 82.

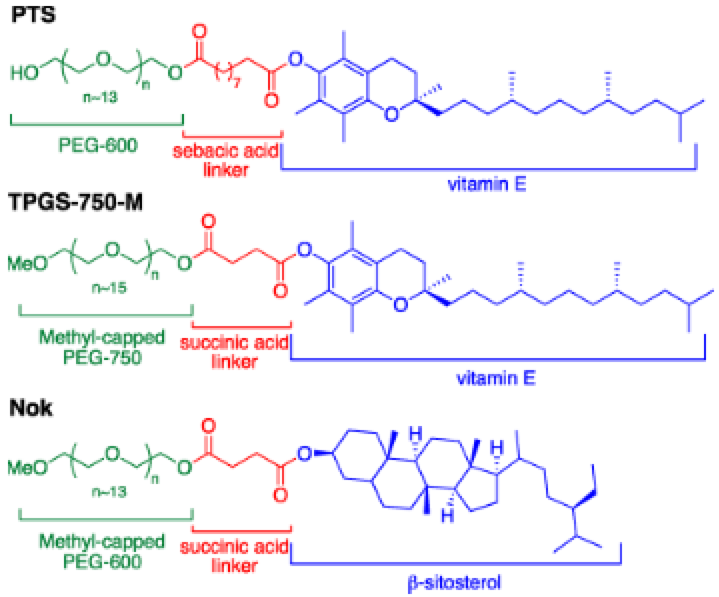
Solvents Guide: What about water?

Chemistry in Water:

Seminal work by Prof. Breslow: Diels-Alder Reaction accelerated «on-water»
Further developement with micellar-type chemistry using Surfactants + catalysis



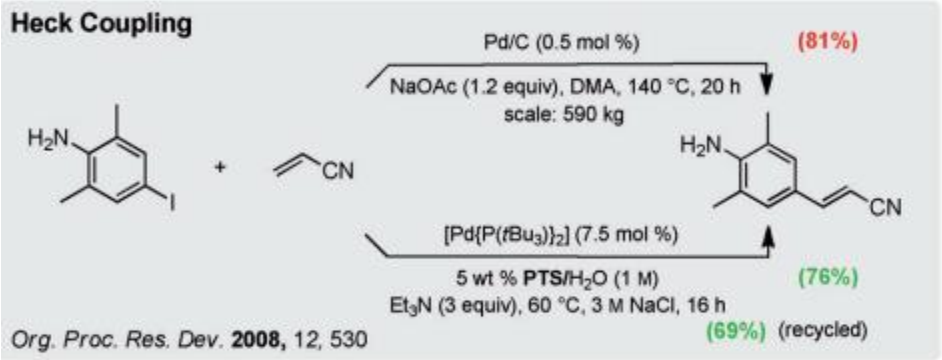




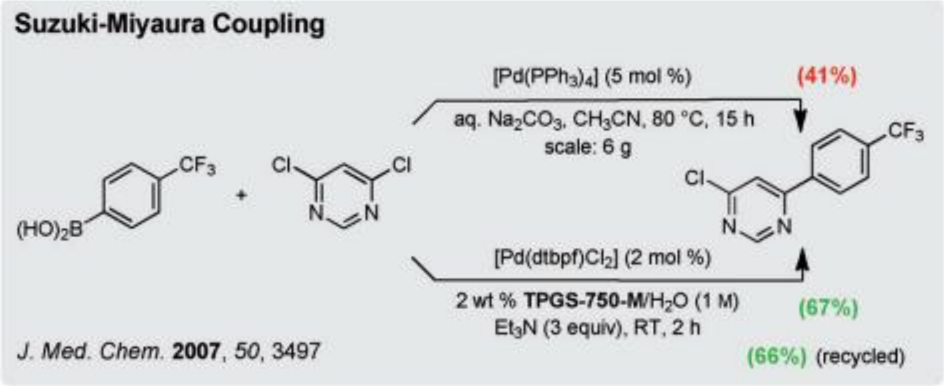
D. C. Rideout and R. Breslow, Hydrophobic acceleration of Diels-Alder reactions, *J. Am. Chem. Soc.* **1980**, *102*, 7816.

Solvents Guide: What about water?

Chemistry in Water:



	based on:	pharma	this work	with recycle
E Factors	total organic solvent	16.7	**2.5**	**2.8**
	aqueous workup included	31.1	**10.2**	**2.8**



	based on:	pharma	this work	with recycle
E Factors	total organic solvent	22.0	**1.9**	**1.9**
	aqueous workup included	50.0	**7.6**	**1.9**

E-Factor calculations: Lipschutz, B. H. *et al. Angew. Chem. Int. Ed.* **2013**, *52*, 10952 & Lipschutz, B. H. *et al. Green Chem.* **2014**, *16*, 3660.
Kitanosono, T. *et al. Chem. Rev.* **2018**, *118*, 679.
Stevens, A. *Synthesis* **2019**, *51*, 2632.
Margery C.-C. *et al. Chem. Eur. J.* **2018**, *24*, 6672 & *Chem. Sci.*, **2021**, *12*, 4237.
Fleck, N *et al. Org. Process Res. Dev.* **2023**, *27*, 822.

Biosynthesis/Biocatalysis/Bio-Based Products

Evaluation of the Impact:

New questions and parameters

Energy consumption
CO_2 Footprint
Supply Chain

Common mistake: Bio-based products are they synonymous with the term “sustainable” ?

Special Issue on Sustainability Metrics of Chemicals from Biomass
https://www.sciencedirect.com/journal/catalysis-today/vol/239/suppl/C

Biosynthesis/Biocatalysis/Bio-Based Products

Nagoya Protocole:

Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity

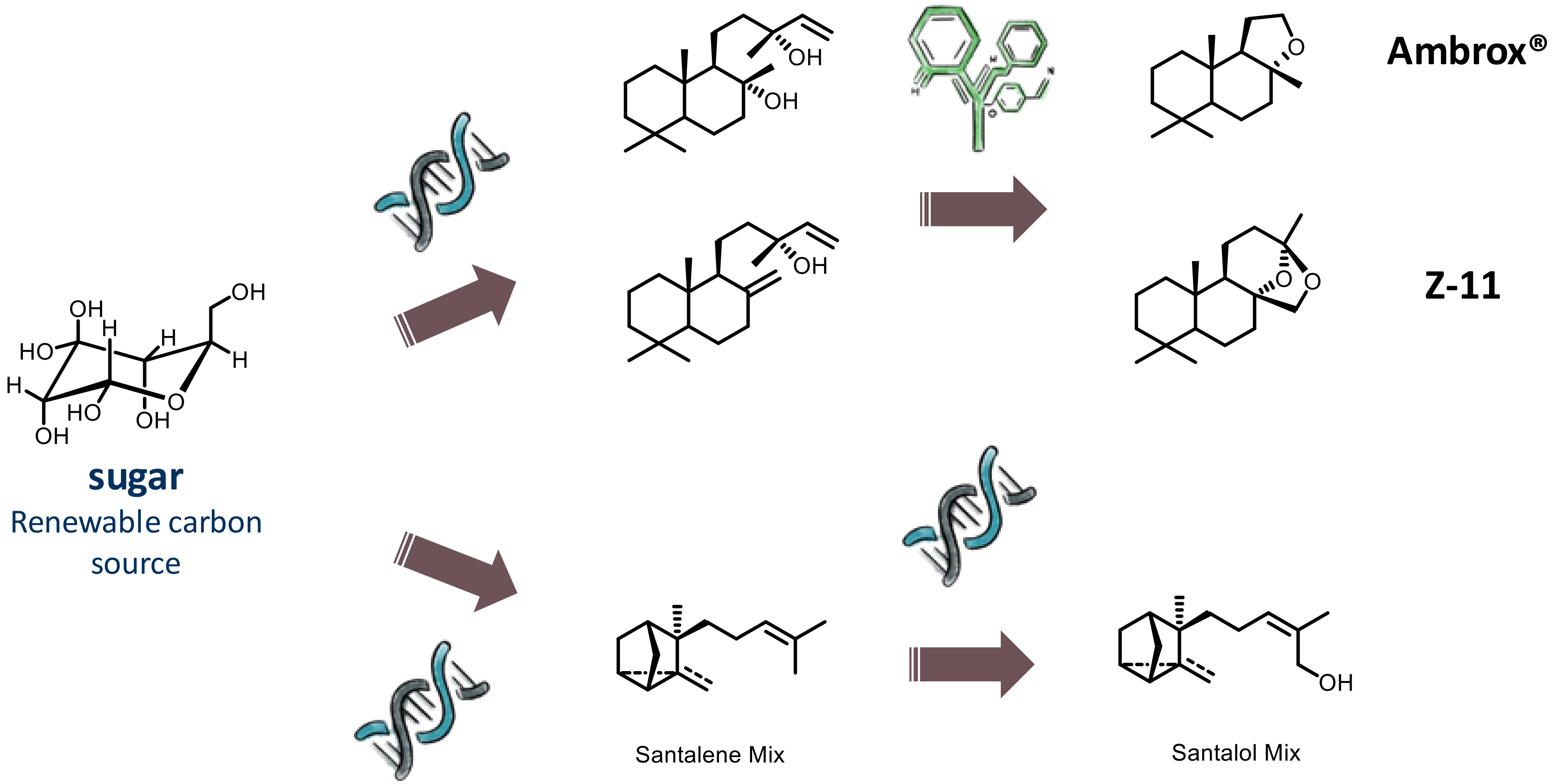
Adopted in 2010
Entered in force in 2014
In 2022, ratified by 137 states

Benefit-sharing obligations
Compliance obligations

https://www.cbd.int/abs/doc/protocol/nagoya-protocol-fr.pdf

Biosynthesis/Biocatalysis/Bio-Based Products

Evaluation of Biotechnology Processes



Schalk, M. *et al. J. Am. Chem. Soc.* **2012**, *134*, 18900.
Concept of Bio-Retrosynthesis: *Nat Chem Biol* **2014**, *10*, 392. https://doi.org/10.1038/nchembio.1494

Biosynthesis/Biocatalysis/Bio-Based Products

Evaluation of Biotechnology Processes: Pros vs Cons

Claim	Rationale
Reduced utilities	Mild reaction conditions (temperature)
Safe operation	Mild reaction conditions (pressure, pH)
Reduced waste	High selectivity
Renewable catalyst	Biocatalyst produced by fermentation based on sugar, air, and water

- **Operates in water (thus replacing organic solvents)**
- **Has highly selective catalysis, including regio- and stereoselectivity (thus reducing E-factors)**
- **Operates in mild conditions, avoiding the need for protection (thus reducing E-factors)**
- **Overcomes the use of some hazardous materials (resulting in improved LCA)**
- **Uses renewable resources (resulting in improved LCA)**
- **Can be modified, that is, the biocatalyst properties can be altered to suit the process (thus improving the ease of processing)**
- **Is rarely endo- or exo-thermic (thus reducing energy requirements)**
- **Provides a high yield as a result of selectivity and mild conditions (thus improving the efficiency of processing)**
- **Is catalytic rather than stoichiometric (thus improving the ease of processing)**

Woodley, J. M. Benchmarking the Sustainability of Biocatalytic Processes in *Handbook of Green Chemistry Volume 11: Green Metrics, First Edition.* Ed. Wiley-VCH, **2018**.
Woodley, J. M. Trends in Biotechnology, **2008**, *26(6)*, 321.

Biosynthesis/Biocatalysis/Bio-Based Products

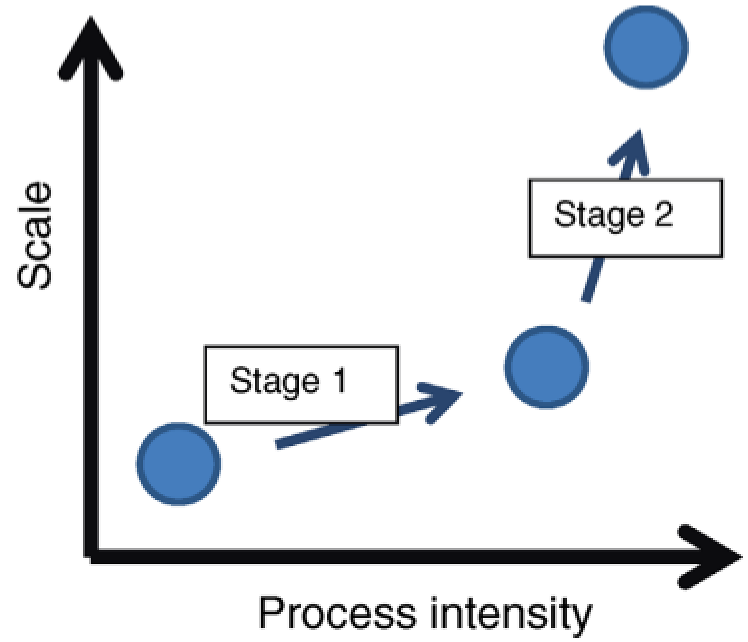
Evaluation of Biotechnology Processes: Pros vs Cons

Performance	Potential limitation
Selective	Enzyme
Reaction rate	Amount of catalyst
	Mass transfer
Reaction yield	Thermodynamics
	Stoichiometry

Woodley, J. M. Benchmarking the Sustainability of Biocatalytic Processes in *Handbook of Green Chemistry Volume 11: Green Metrics, First Edition.* Ed. Wiley-VCH, **2018**.

Biosynthesis/Biocatalysis/Bio-Based Products

Evaluation of Biotechnology Processes



Stage	Benchmarking objective	Methodology
1	Route feasibility	*In silico* metrics: AE; CME
2	Biocatalyst and reaction development	*In vitro* metrics: PMI; SI; WI; E-factor

Woodley, J. M. Benchmarking the Sustainability of Biocatalytic Processes in *Handbook of Green Chemistry Volume 11: Green Metrics, First Edition.* Ed. Wiley-VCH, **2018**.

Biosynthesis/Biocatalysis/Bio-Based Products

Metrics used for Bioprocesses:

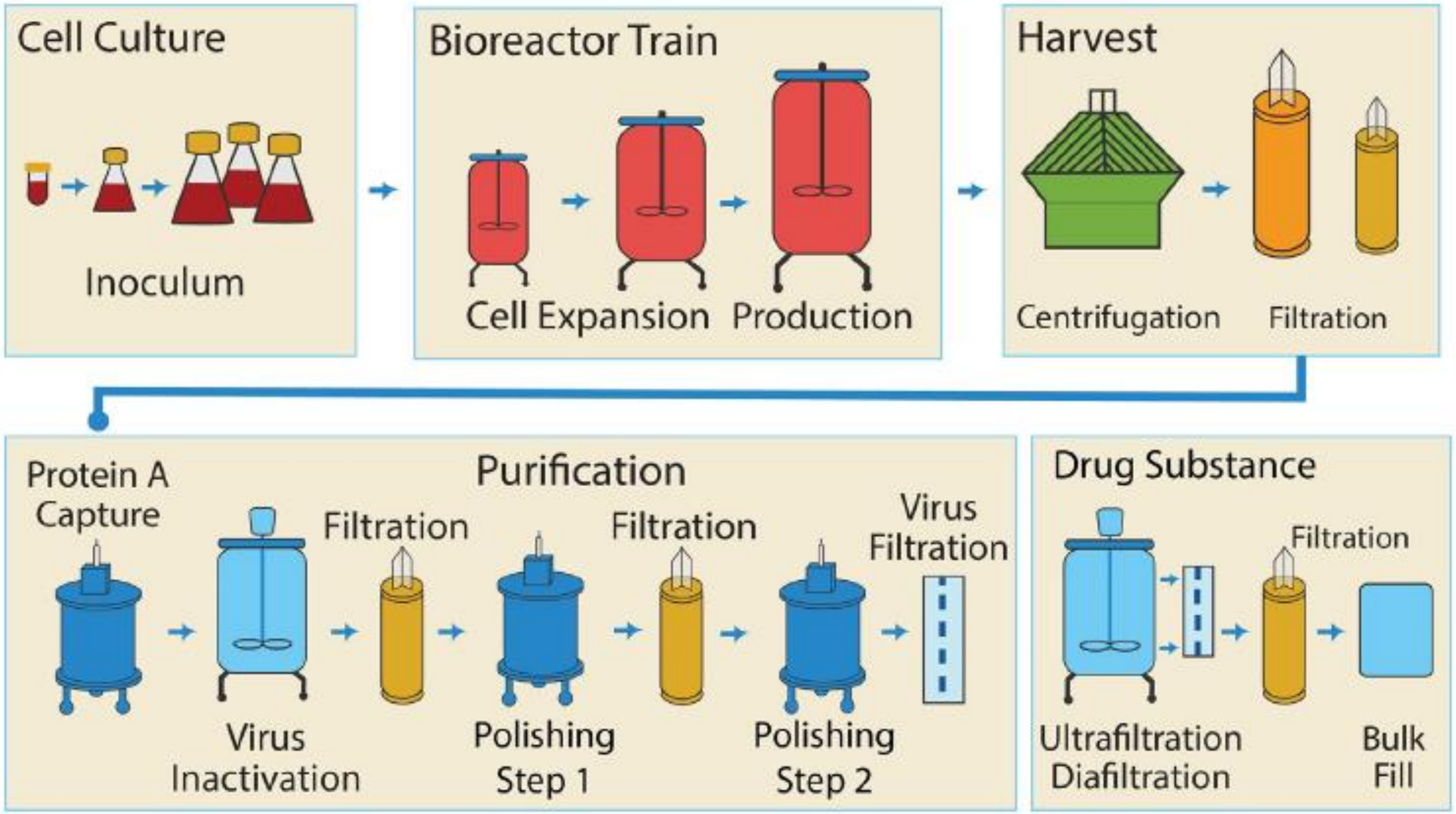
Metric	Definition
Economic metrics	
Productivity ($g\,l^{-1}\,h^{-1}$)	Amount of product made as a function of the reactor volume and time
Yield of product on substrate ($g\,g^{-1}$)	Amount of product (grams) made as a function of the amount of substrate (grams) added in the reaction
Turnover ($mol\,mol^{-1}$)	Amount of product made as a function of the amount of biocatalyst added in the reaction
Green chemistry metrics	
Atom economy ($g\,mol^{-1}$ per $g\,mol^{-1}$)	Molecular weight of the desired product as a function of the sum of the molecular weight of all products
E factor ($g\,g^{-1}$)	Amount of waste made as a function of the amount of product made
C factor ($g\,g^{-1}$)	Amount of CO_2 equivalents as a function of the amount of product made
Process mass intensity ($g\,g^{-1}$)	Amount of raw material input as a function of the amount of desired product made

Bell, E.L., Finnigan, W., France, S.P. *et al.* Biocatalysis. *Nat Rev Methods Primers* **2021**, *1*, 46.
Woodley, J. M. New frontiers in Biocatalysis for sustainable synthesis. *Curr. Opin. Green. Sustain. Chem.* **2020**, *21*, 22.

Biopharmaceuticals/Biologics

Metrics used for biologics:

Cleaning and sanitization but increases the amount of waste Generated
Highly purified water: Energy!
65% of the carbon footprint is attributable to the energy required to maintain the clean room facility that houses the operation
Single use systems (SUS) made of mixed plastics which are sterilized by gamma irradiation



Budzinski, K. *et al. New Biotechnology* **2019**, *49(25)*, 37-42.
Argoud, S. et al. *Current Opinion in Green and Sustainable Chemistry* **2022**, *35,* 100614.

For the energy of water purification: Cataldo, A. L. *et al.* Water related impact of energy: cost and carbon footprint analysis of water for biopharmaceuticals from tap to waste. *Chem Eng Sci X* **2020**, *8*, 100083. https://doi.org/10.1016/j.cesx.2020.100083

Biosynthesis/Biocatalysis/Bio-Based Products

Further Developements for Bringing Benefits to Sustainability of Biocatalysis:

	Sustainability Benefits
Reaction Intensification Flow Biocatalysis Multi-step Catalysis	Reduced Downstream costs Reduced *E* Factor Reduction in Reactor Footprint Better control Reduction in Isolation steps and Solvent swap

Woodley, J. M. New frontiers in Biocatalysis for sustainable synthesis. *Curr. Opin. Green. Sustain. Chem*. **2020**, *21*, 22.

Bio-Based Products

Hybridised sustainability metrics for use in life cycle assessment of bio-based products: resource effeciency and circularity

Feedstock Intensity: $$\text{FI} = \frac{M_{raw\,Mat}}{M_{main\,Prod} + M_{co\,Prod}}$$

Circular Process Feedstock Intensity: $$CPFI = \frac{M_{raw\,mat}}{M_{Main\,Prod} + MCo_{\,Prod} + MRec_{\,Mat}}$$

Also the Process Material Circularity, Energy Intensity, Circular-Process Energy Intensity, …

Lokesh, K. *et al.* Hybridised sustainability metrics for use in life cycle assessment of bio-based product *Green Chem.*, **2020**, *22*, 803.
Sheldon, R. A. *ACS Sustainable Chem. Eng.* **2018**, *6*, 32–48.

Renewability

Renewables Intensity

$$RI = \frac{\sum m(All\ Renewably\ derived\ materials\ used)}{m(Product)}$$

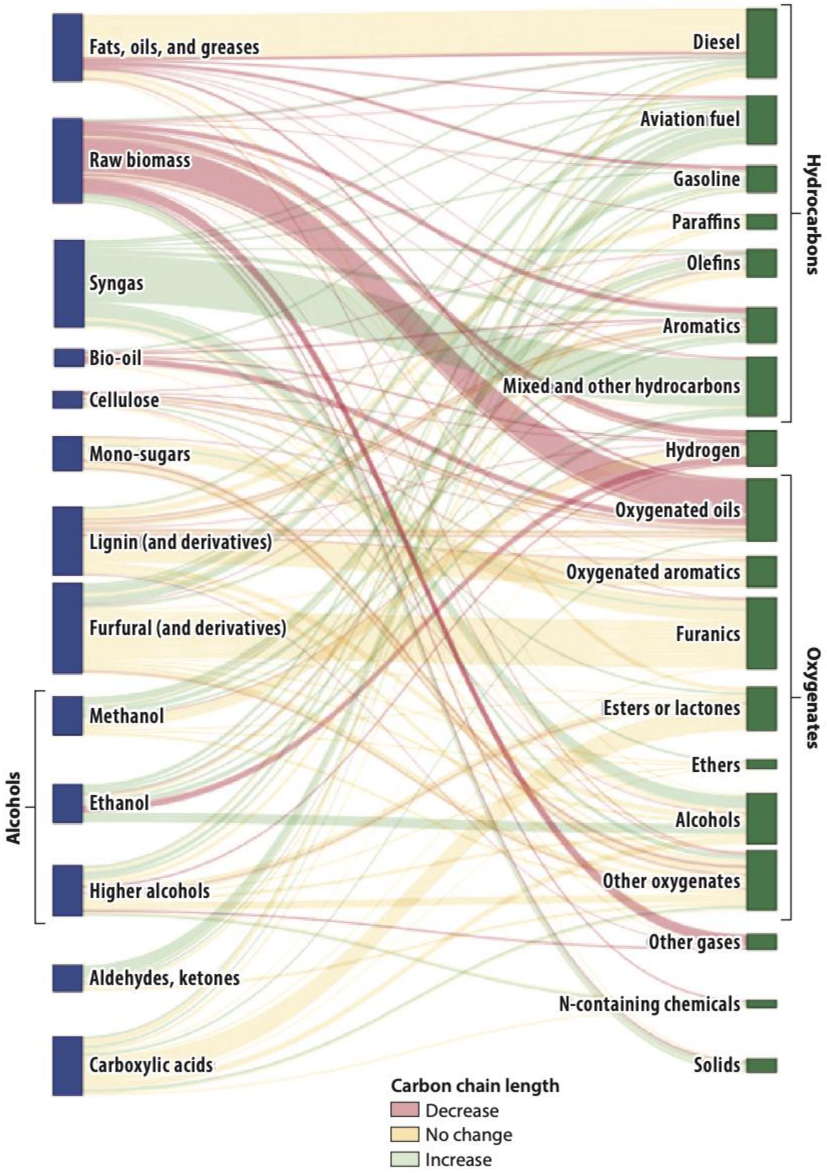
Optimum Value= 1.

$$R\ percentage = \frac{RI}{PMI} \times 100$$

Jimenez-Gonzalez, C. *et al.* Evaluating the ''Greenness'' of chemical processes and products in the pharmaceutical industry—a green metrics primer *Chem. Soc. Rev.* **2012**, *41*, 1485–1498.
Ruiz-Mercado, G. J. *et al. Ind. Eng. Chem. Res.* **2012**, *51*, 2309-2328.

Bio-Based Products

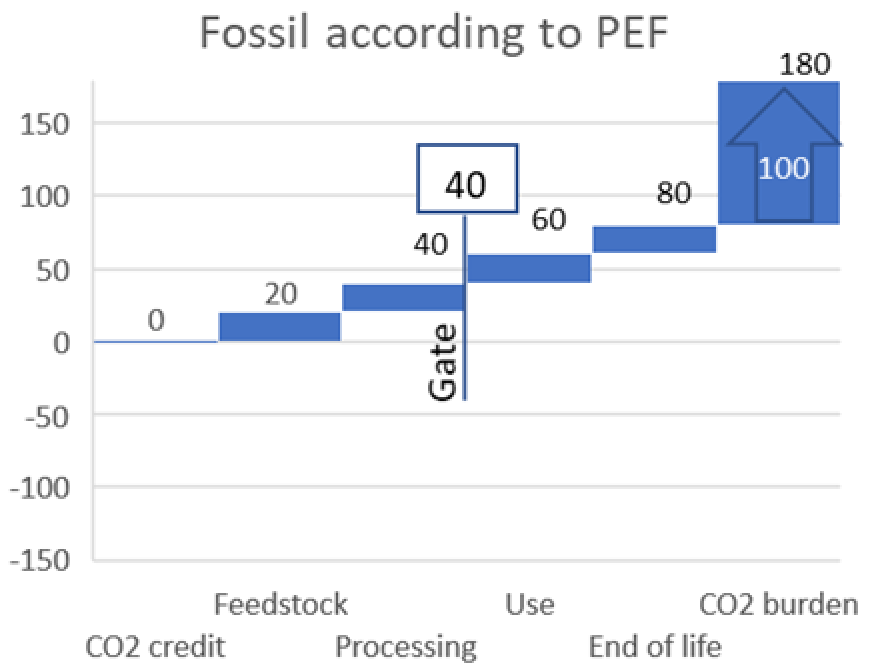
Feedstocks and products from scholarly research papers employing thermal catalysis for upgrading sustainable feedstocks published in 2023 (402 papers)

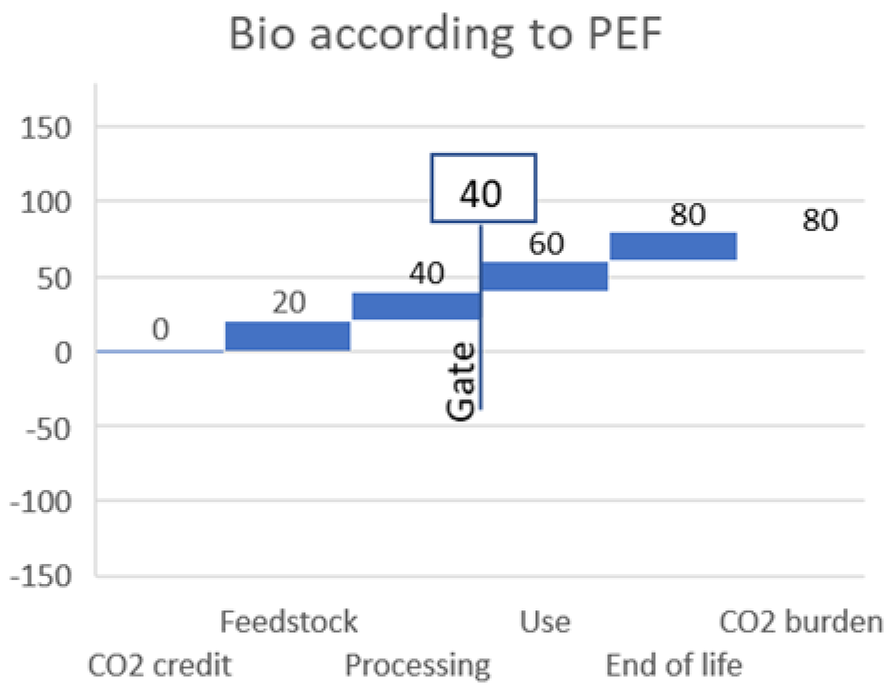


J. N. Hall *et al.* *Annu. Rev. Chem. Biomol. Eng.* **2025**, *16*, 371–408.

Bio-Based Products

Carbon footprint of Bio-based Products: proposition of the CEFIC [European Chemical Industry Council]

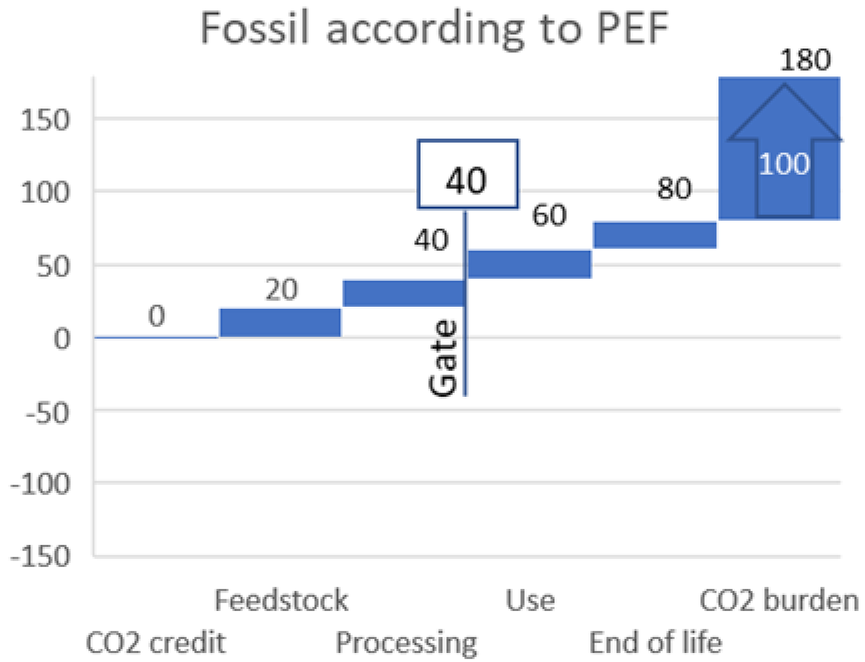


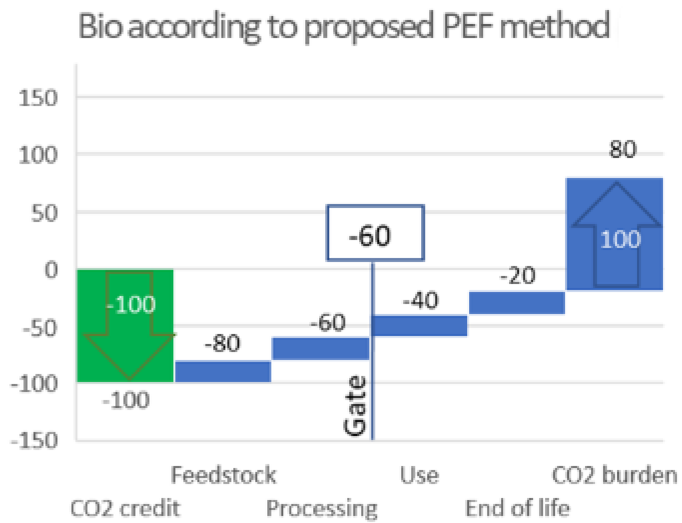


https://cefic.org/media-corner/newsroom/cefics-counterproposal-to-assess-the-carbon-footprint-of-bio-based-products/

Bio-Based Products

Carbon footprint of Bio-based Products:





https://cefic.org/media-corner/newsroom/cefics-counterproposal-to-assess-the-carbon-footprint-of-bio-based-products/

Bio-Based Products

Carbon footprint of Bio-based Products:

Facilitate the development and adoption of international sustainability indicators for Biobased Products that are science-based, unambiguous and validated. These should consider factors such as:

- Energy balance, including non-renewable and renewable energy use.
- All greenhouse gas reduction over product life cycles.
- Bio-based content as an indicator of renewability.
- Anticipated product life.
- Water and solvent use during the different stages of production and impacts on biodiversity during feedstock production and subsequent processing.
- Direct and indirect land use for feedstock production.
- All aspects of end of product life.
- Conventional as opposed to alternative bio-based production economics.
- Impact on human and environmental health.

https://legalinstruments.oecd.org/public/doc/283/283.en.pdf

István T. Horváth *et al.* Sustainability Metrics for Biomass-Based Carbon Chemicals *ACS Sustainable Chem. Eng.* 2017, *5*, 2734.

Upcycling of Waste Stream

Different Methods for Different Wastes:

2 main types of waste:

Bio-waste: from agriculture, paper industry, …

«chemical» waste: Polymers, …

Different types of extraction methods: Organic Solvents, Supercritical CO_2, Steam, Mechanical extraction,…

https://www.firmenich.com/fragrance/blog-article/scents-and-sustainability

Waste Valorization

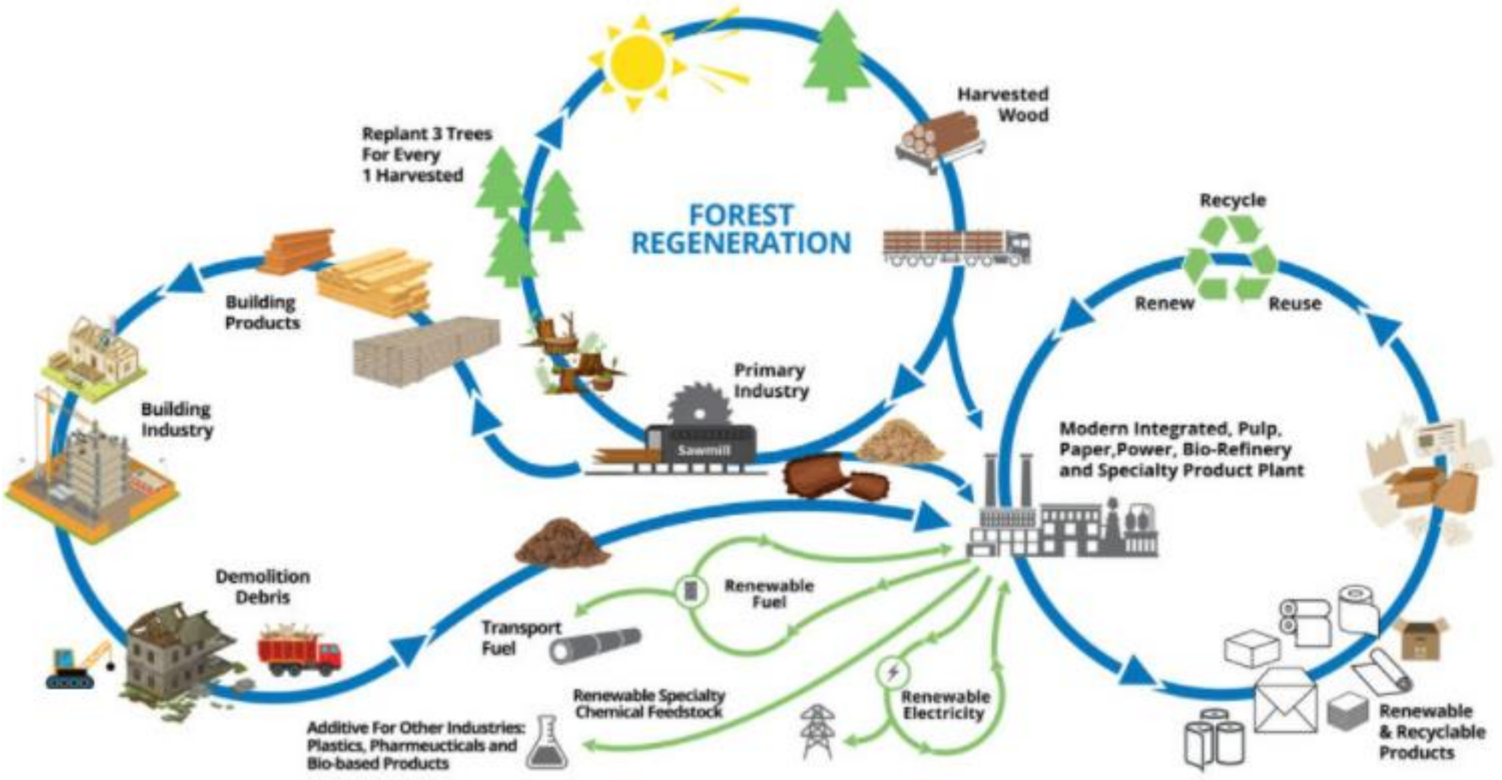
New metrics proposed:

Waste Factor: $$\mathrm{WF} = \frac{M_{Tot\,Waste}}{M_{Prod} + M_{co\,Prod}}$$

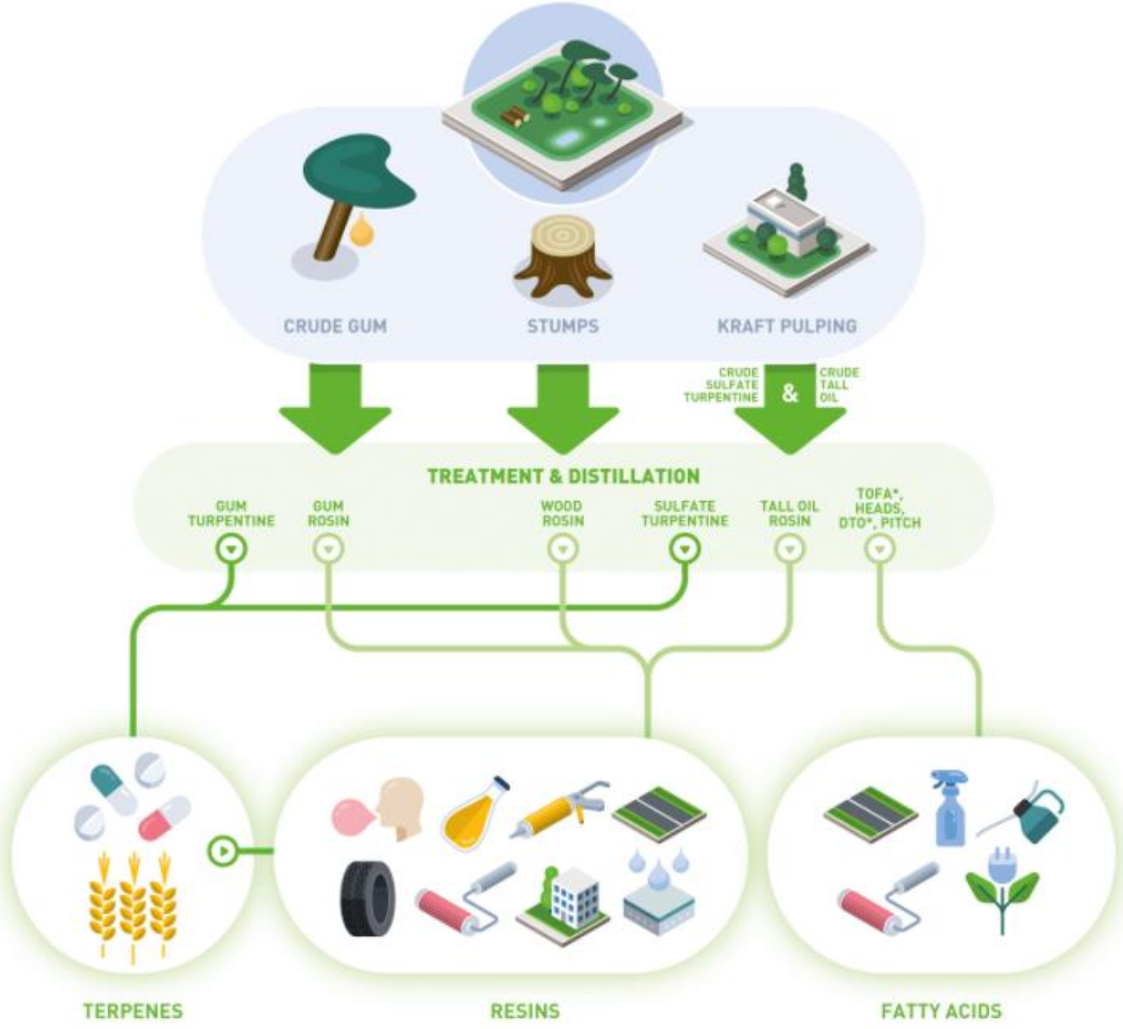
Circular Process Waste Factor: $$CPWF = \frac{M_{Tot\,Waste}}{M_{Prod} + MCo_{\,Prod} + MRec_{\,Mat}}$$

Lokesh, K. *et al.* Hybridised sustainability metrics for use in life cycle assessment of bio-based product *Green Chem.*, **2020**, *22*, 803.
Sheldon, R. A. *ACS Sustainable Chem. Eng.* **2018**, *6*, 32–48.

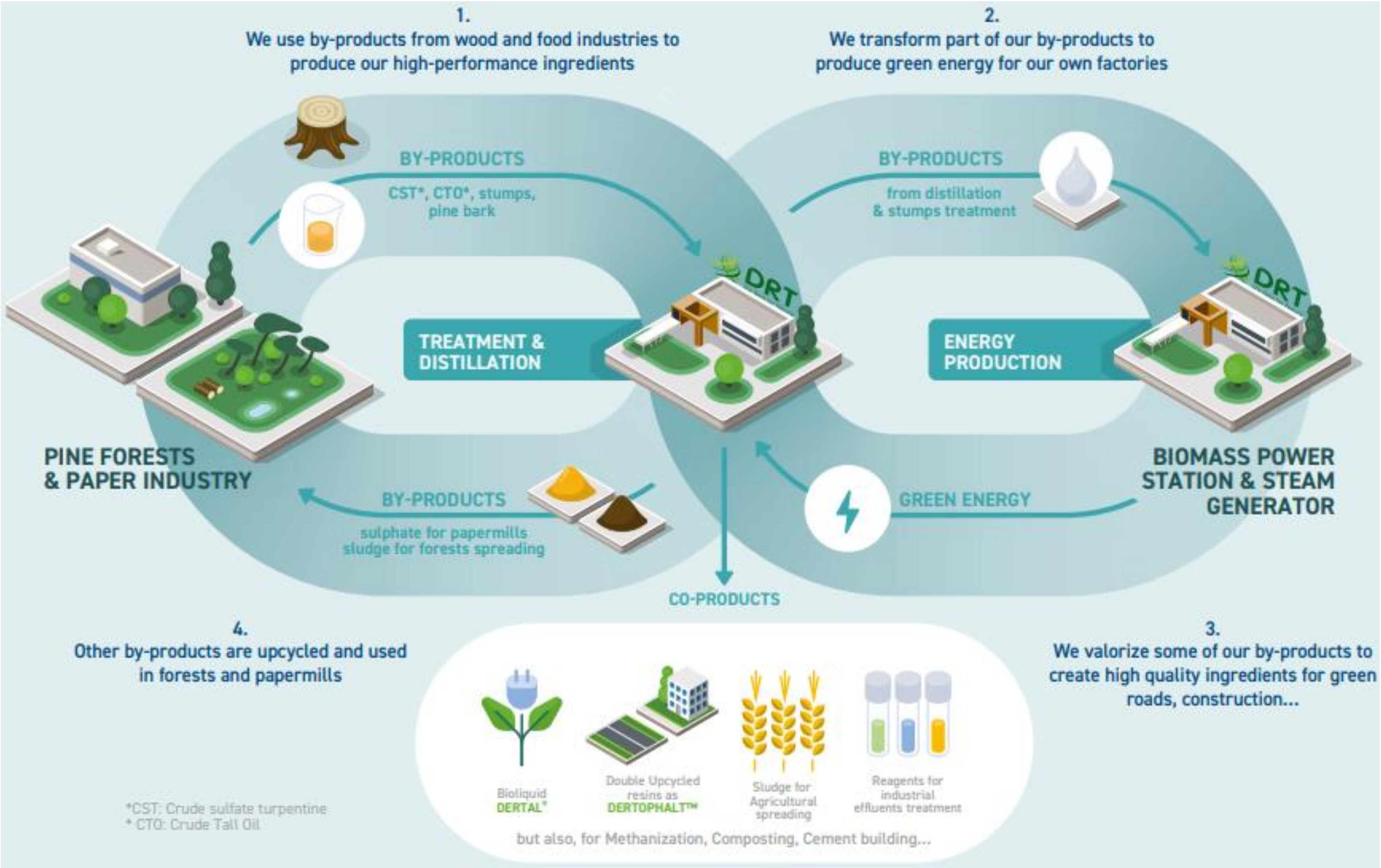
From Paper Industry



From Paper Industry

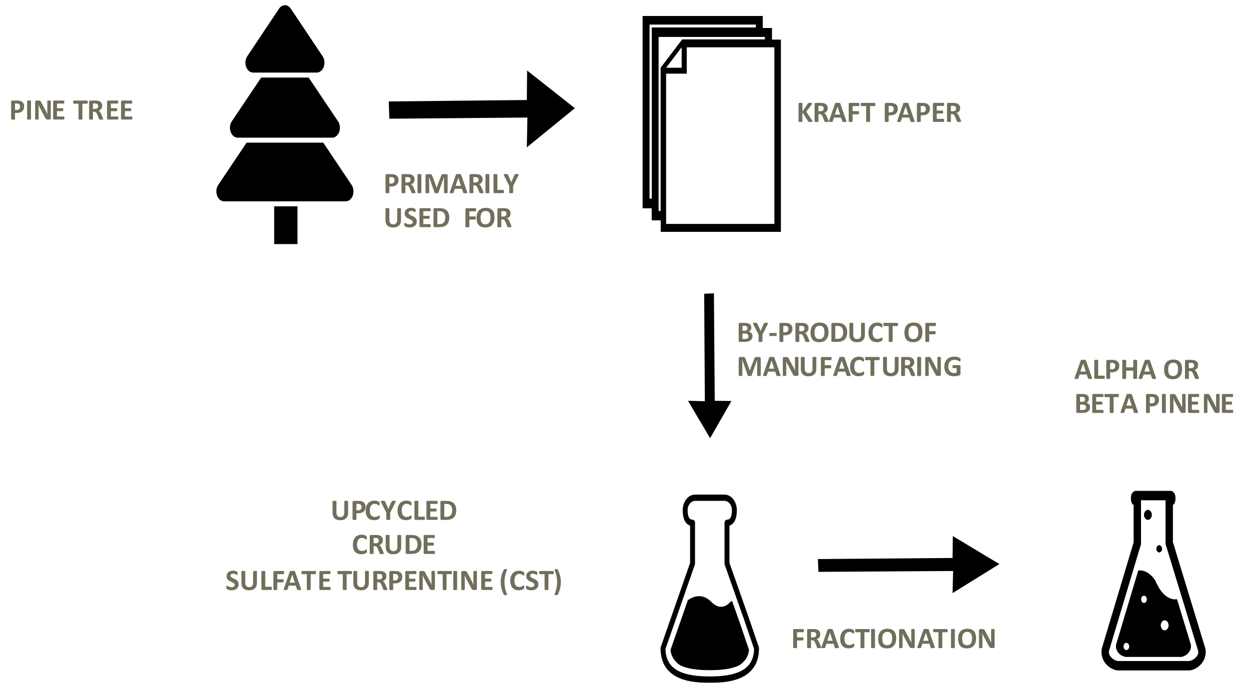


Circularity in practice: Vieille-St-Giron



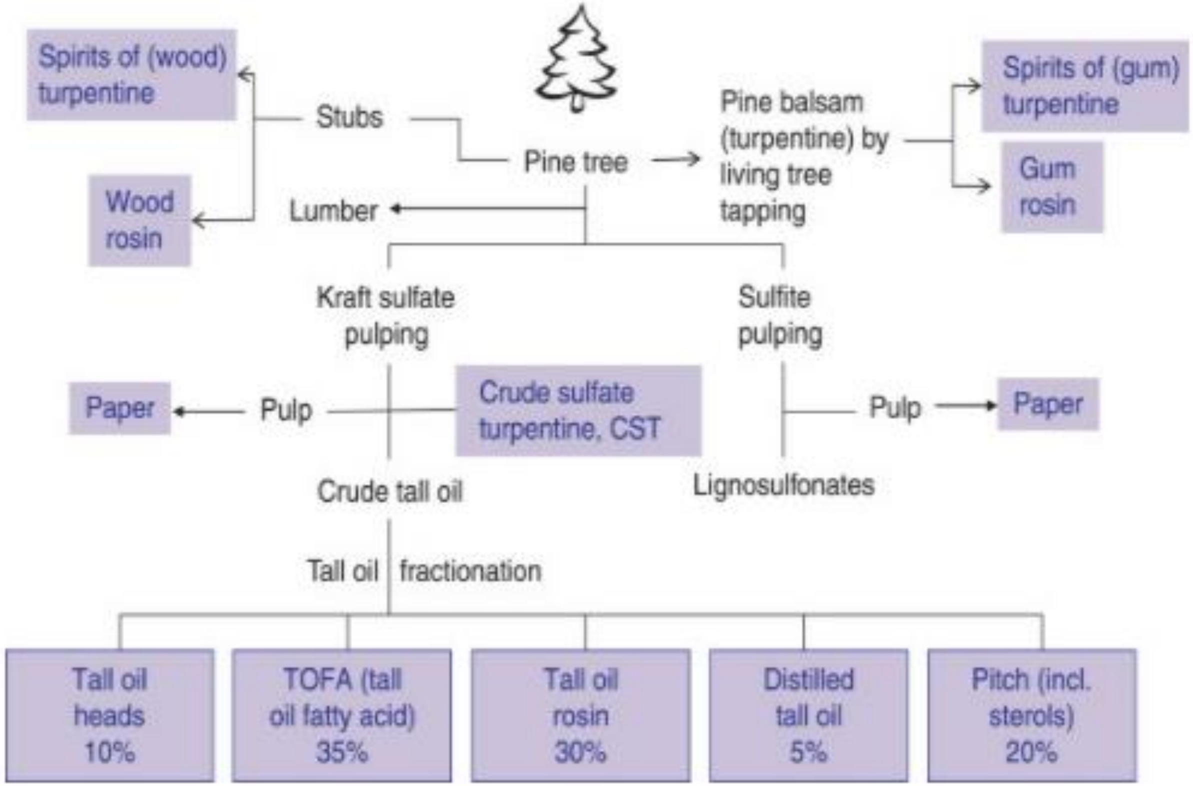
https://www.firmenich.com/sites/default/files/ESGReportFY22.pdf

Circularity in practice: Vieille-St-Giron



Principle 7:
Renewable feedstock

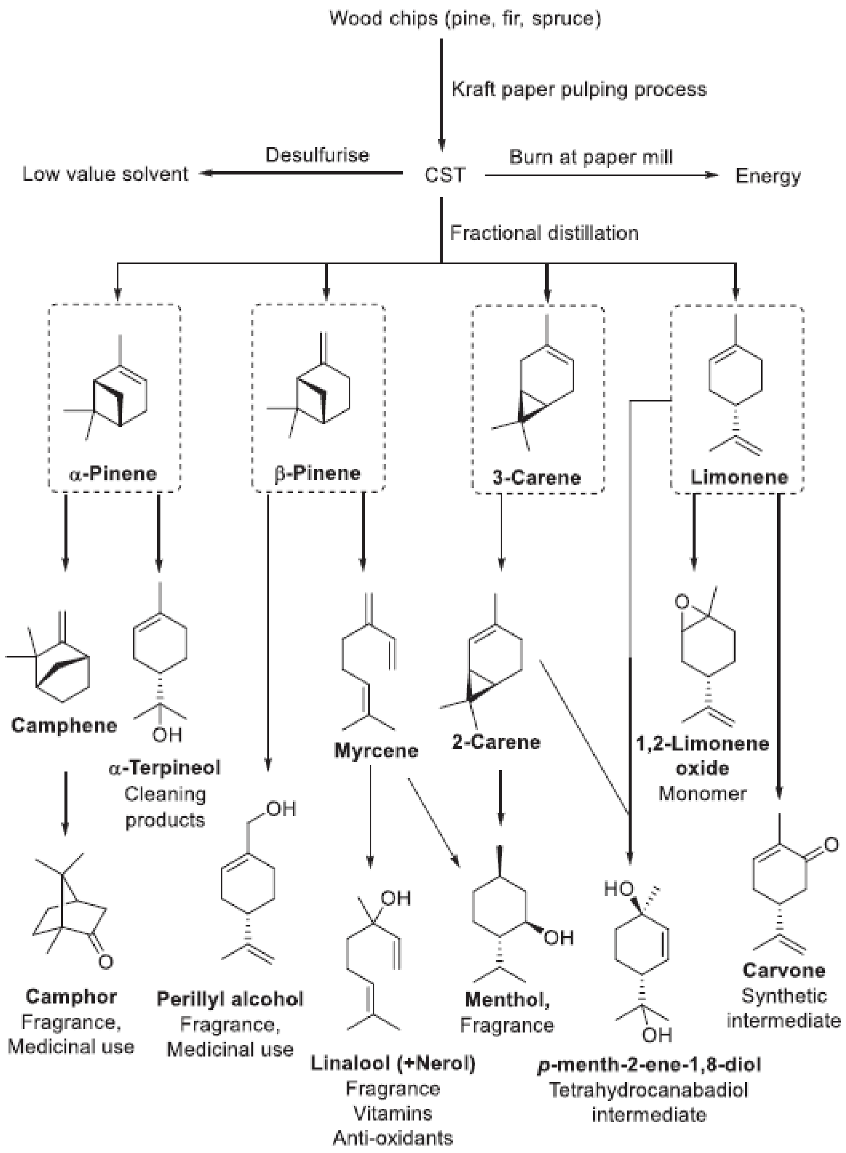
From Paper Industry



Chap. 17 Biermann's Handbook of Pulp and Paper (Third Edition), Volume 1: Raw Material and Pulp Making, 2018, Pages 425-451

From Paper Industry

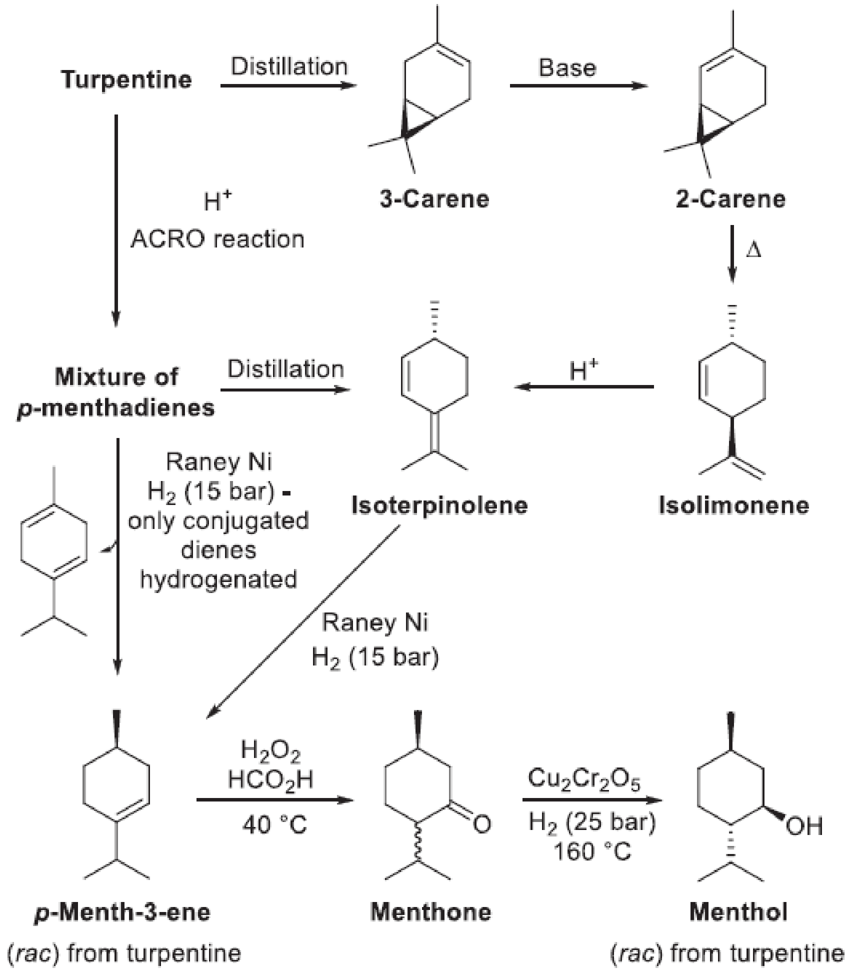
High Value Chemicals:



Tibbetts, j. D.; Bull, S. D. *Adv. Sustainable Syst*. **2021**, *5*, 2000292.

From Paper Industry

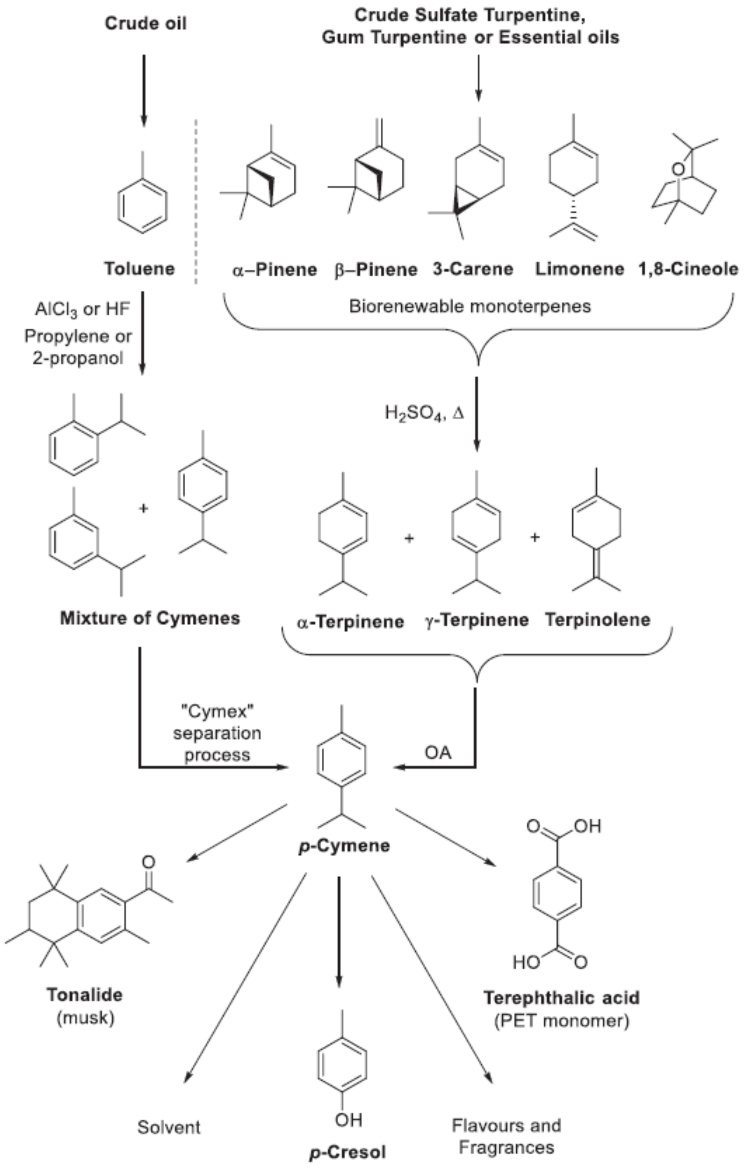
High Value Chemicals:



Tibbetts, j. D.; Bull, S. D. *Adv. Sustainable Syst*. **2021**, *5*, 2000292.

From Paper Industry

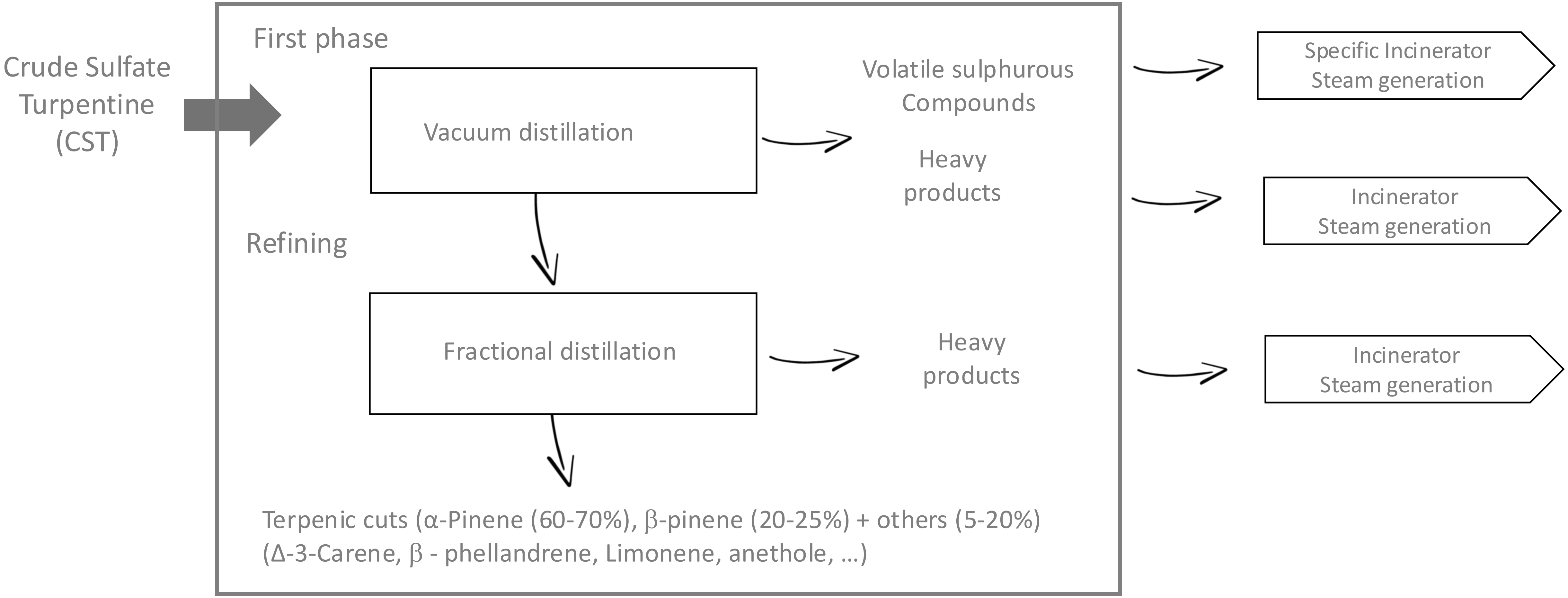
High Value Chemicals:



Tibbetts, j. D.; Bull, S. D. *Adv. Sustainable Syst*. **2021**, *5*, 2000292.

From Paper Industry

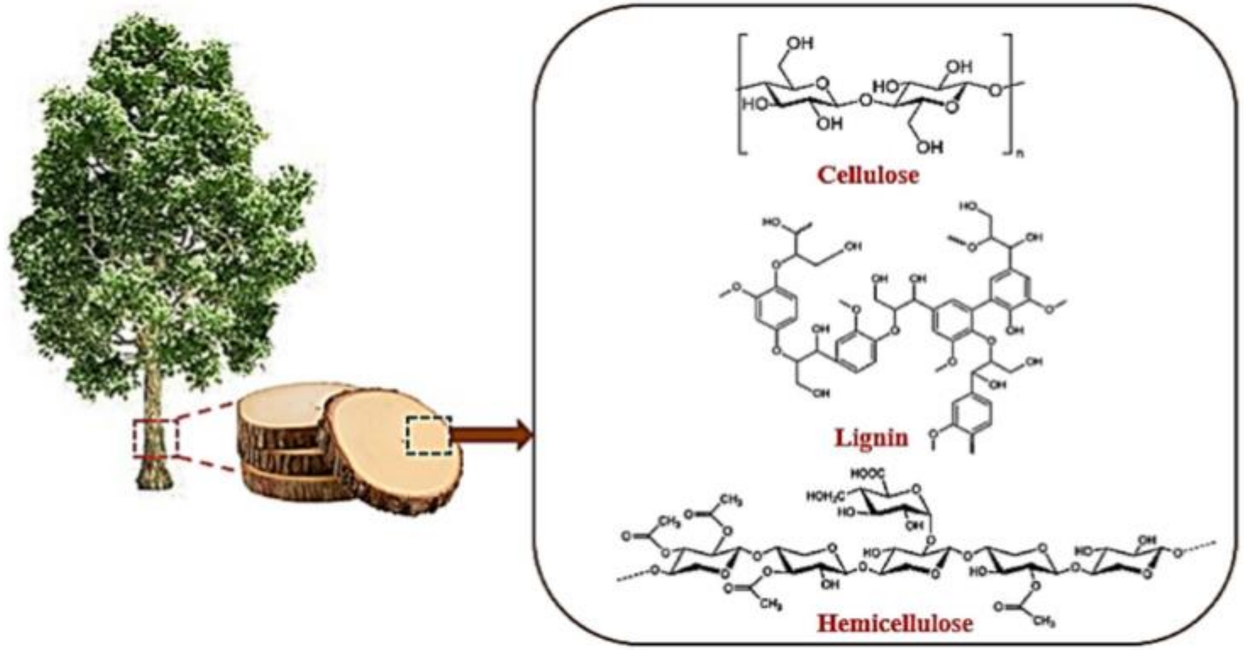
High Value Chemicals:

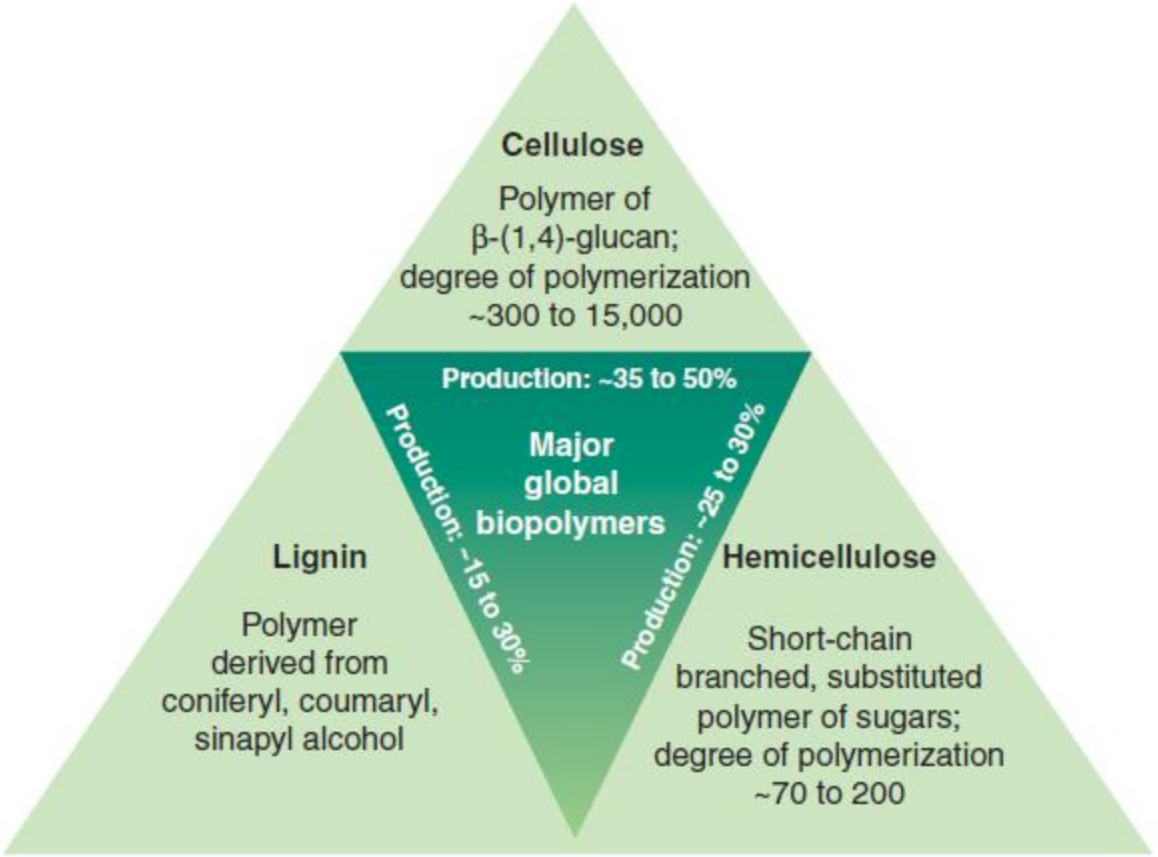


M. Reiter *et al.*, *Chimia* **2021**, *75*, 780.

Key Global Biomass Resources

Agricultural residues, wood, and herbaceous energy crops:

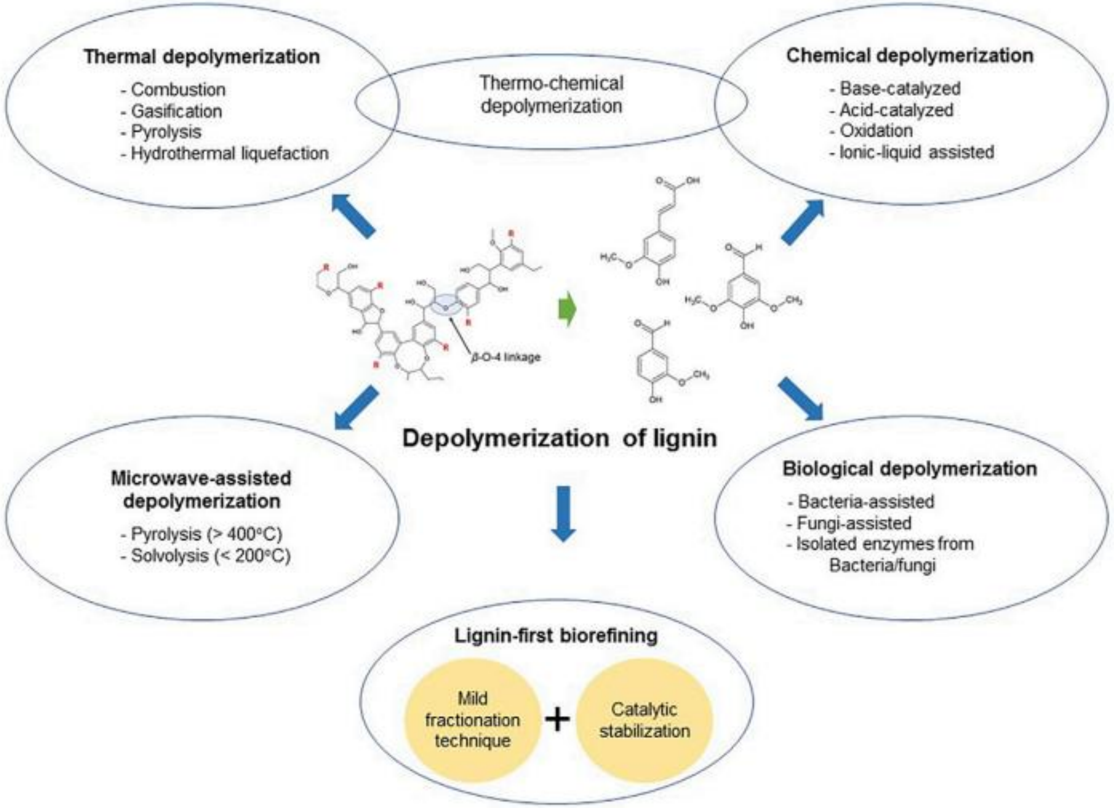


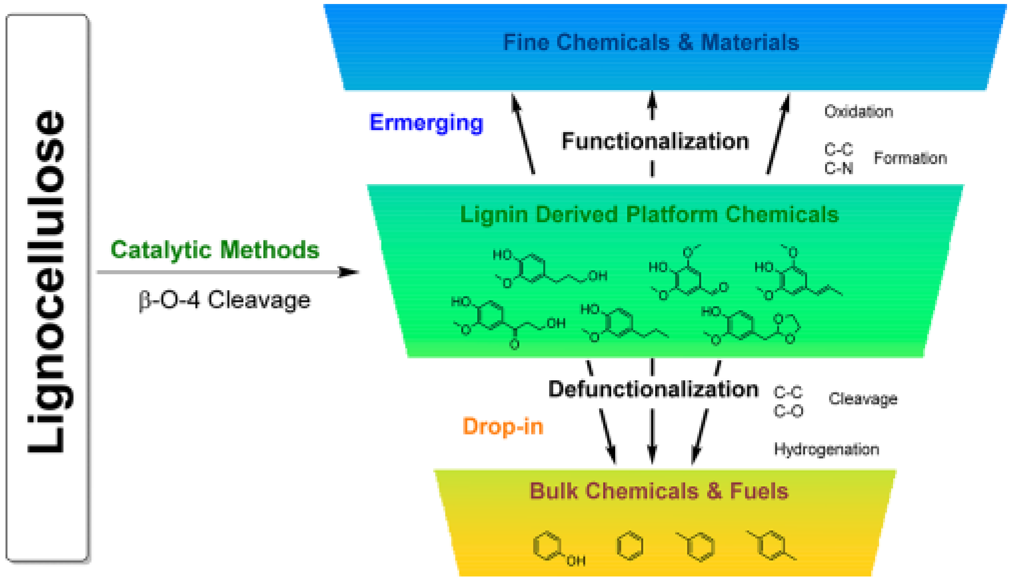


Ragauskas,, A. J. *et al. Science*, **2006**, *311 5760.*
The Path Forward for Biofuels and Biomaterials

From Lignin

Depolymerization of Lignin:

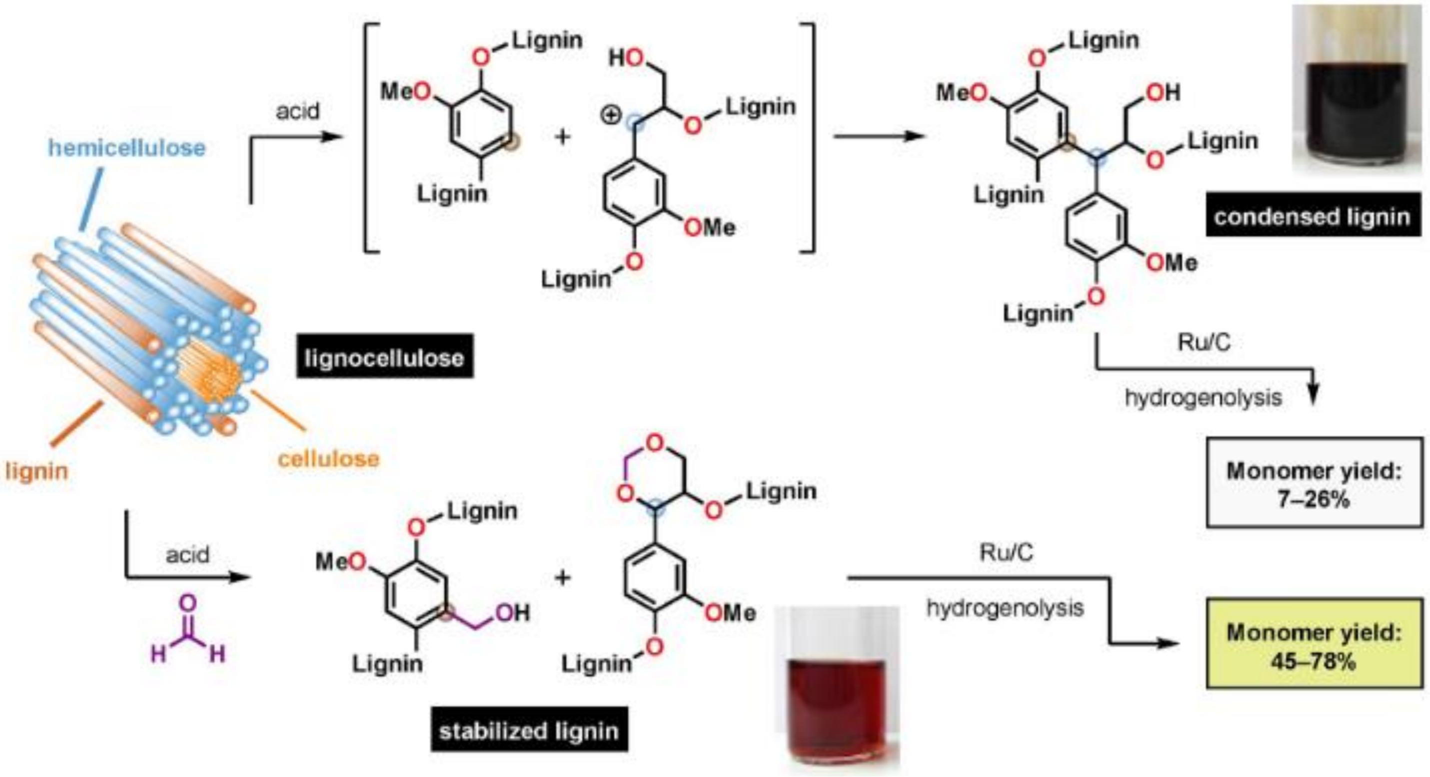




Zhou, N. et al. A Review: Depolymerization of Lignin to Generate High-Value Bio-Products: Opportunities, Challenges, and Prospects. Front. Energy Res. 9:758744. doi: 10.3389/fenrg.2021.758744

From Lignin

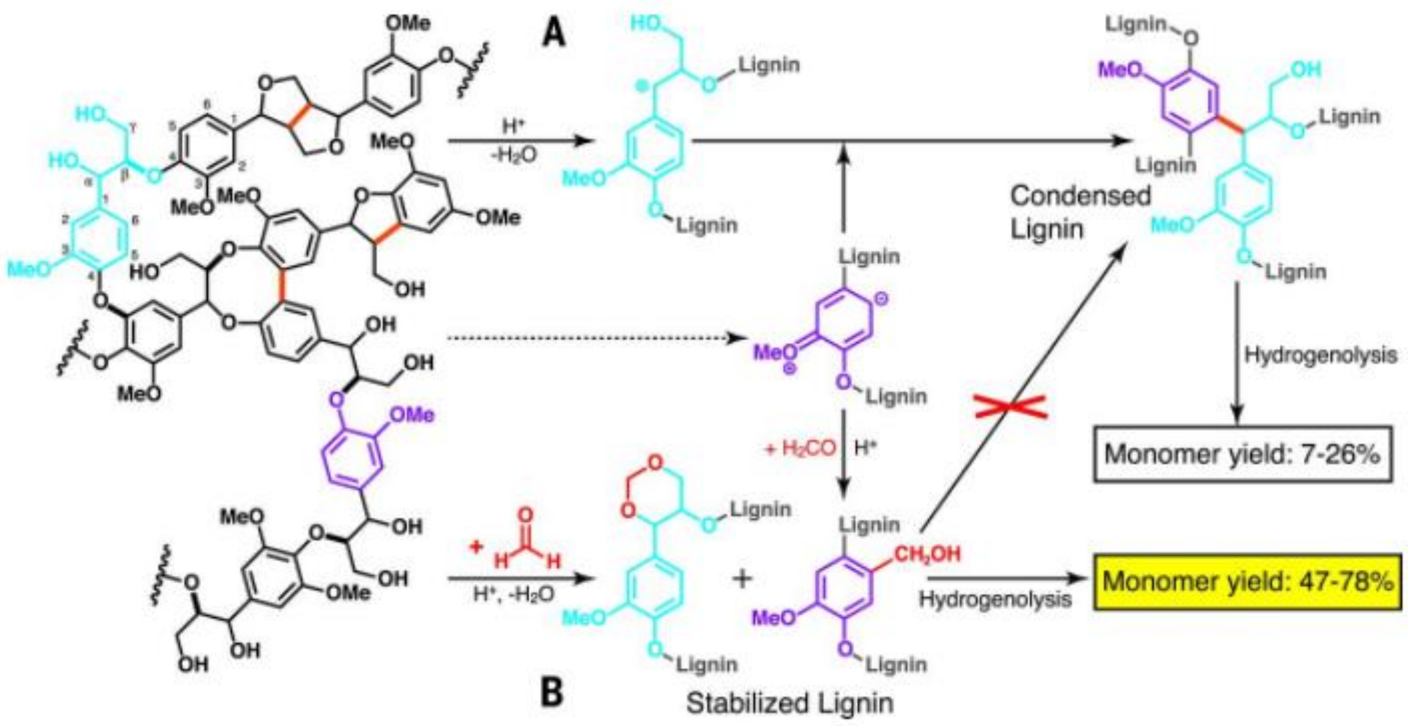
One Example from Bloom Biorenewables:



Kärkäs, M. D. *ChemSusChem* **2017**, *10*, 2111.

From Lignin

One Example from Bloom Biorenewables:

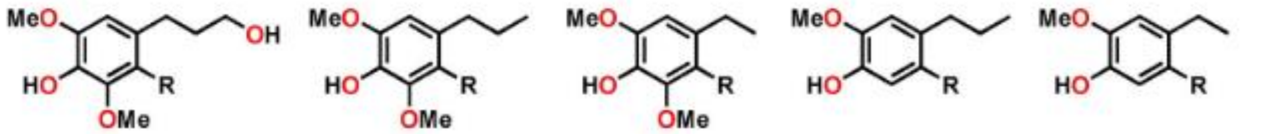


Luterbacher, J. S. *& co. Science* **2016**, *354*, 329.

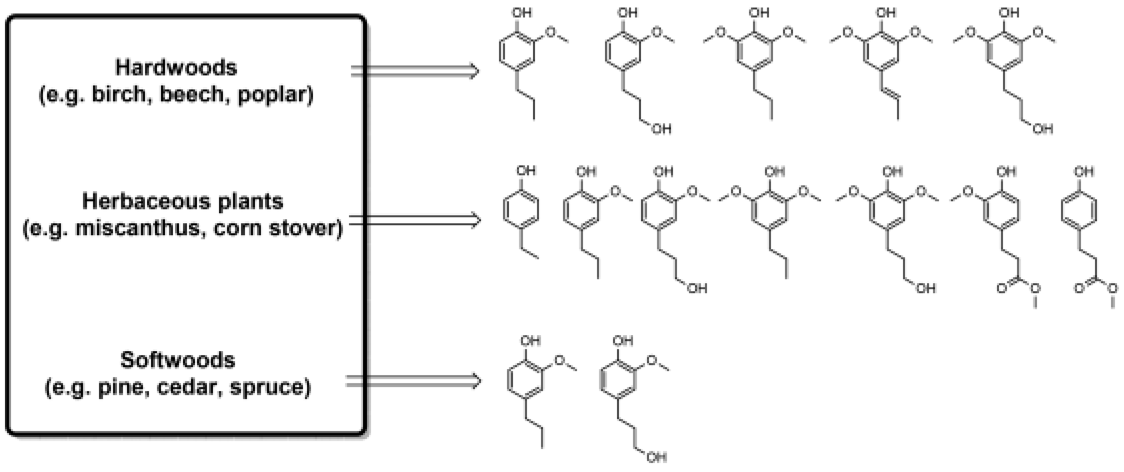
From Lignin

High Value Chemicals:

Product distribution



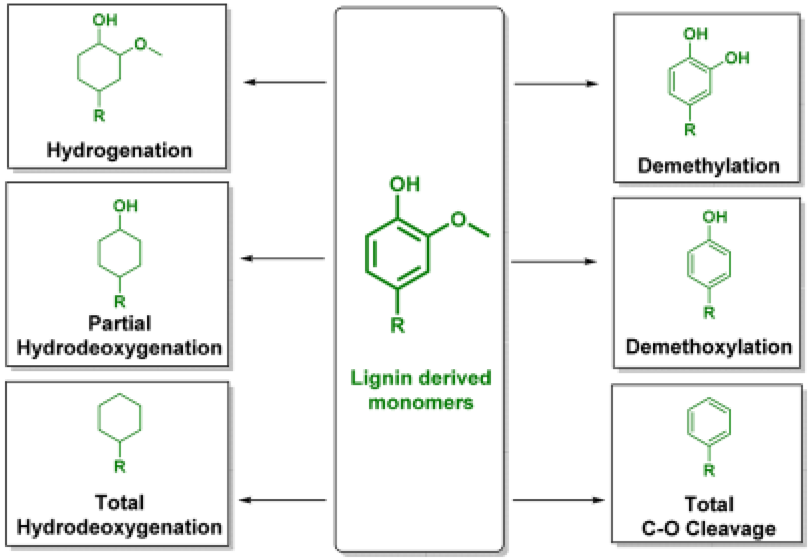
Beech wood[a] (F5H poplar[b])	**4a**: R = H **4b**: R = Me	**5a**: R = H **5b**: R = Me	**8a**: R = H **8b**: R = Me	**7a**: R = H **7b**: R = Me	**9a**: R = H **9b**: R = Me
with formaldehyde	**4a**, 5.67% (16.45%) **4b**, 3.60% (9.08%)	**5a**, 13.31% (18.57%) **5b**, 9.44% (8.97)	**8a**, 2.05% (15.24%) **8b**, 1.07% (5.50%)	**7a**, 7.01% (1.98%) **7b**, 2.27% (0.65%)	**9a**, 0.64% (1.22%) **9b**, – (–)
without formaldehyde	**4a**, 2.00% (2.57%) **4b**, – (–)	**5a**, 1.82% (5.48%) **5b**, – (–)	**8a**, 2.07% (14.86%) **8b**, – (–)	**7a**, 0.66% (–) **7b**, – (–)	**9a**, 0.55% (1.31%) **9b**, – (–)

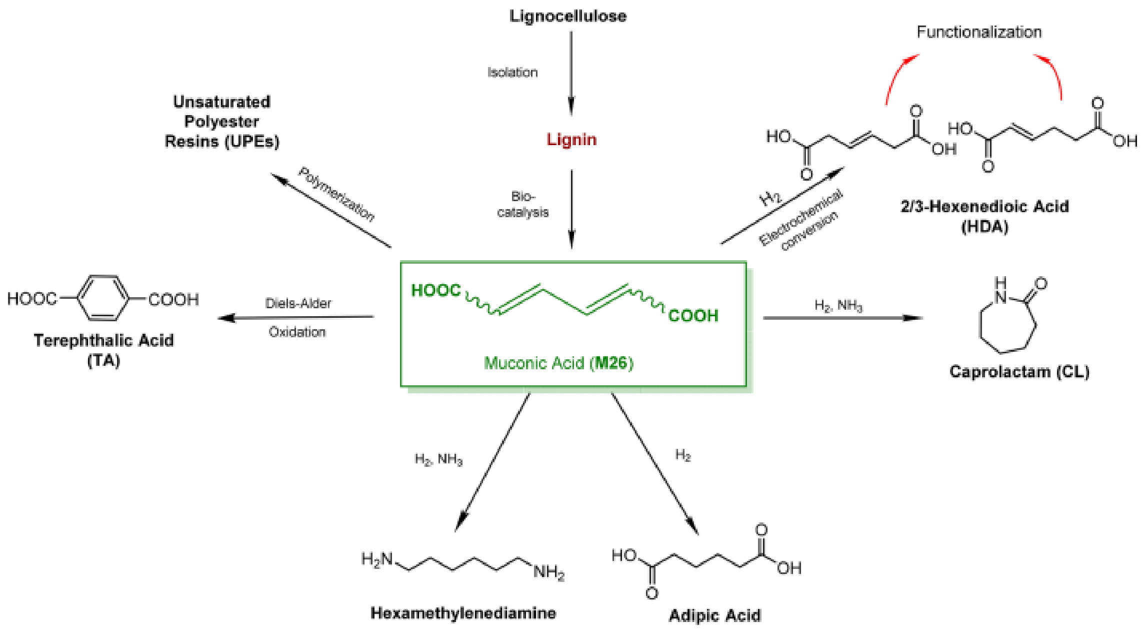


Luterbacher, J. S. *& co. Science* **2016**, *354*, 329.
Kärkäs, M. D. *ChemSusChem* **2017**, *10*, 2111.
Tibbetts, j. D.; Bull, S. D. *Adv. Sustainable Syst*. **2021**, *5*, 2000292.

From Lignin

High Value Chemicals:

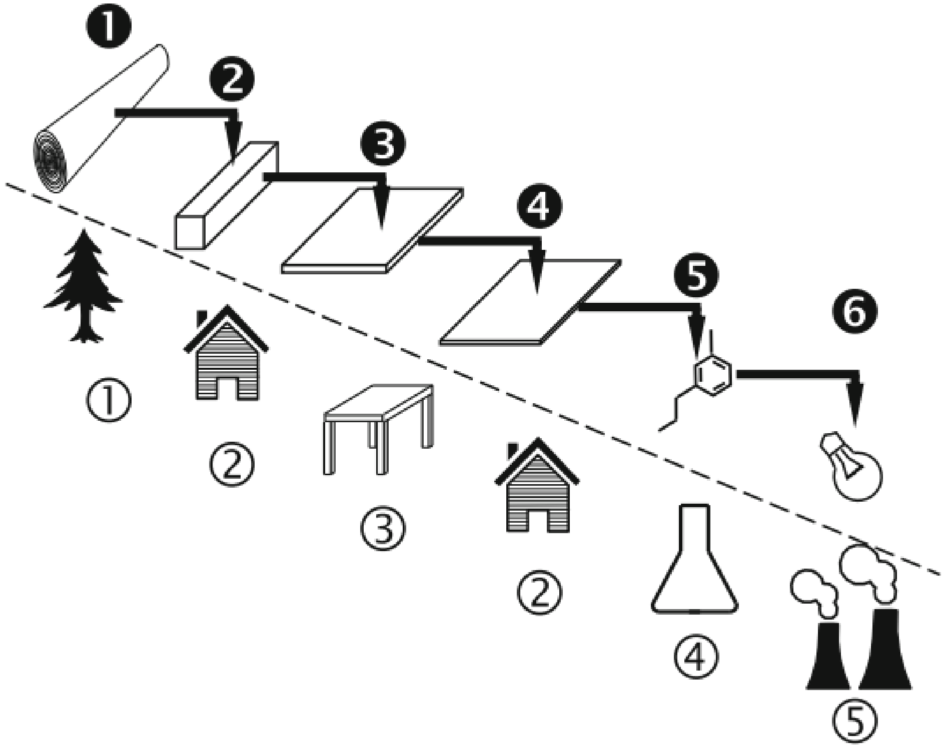




Kärkäs, M. D. *ChemSusChem* **2017**, *10*, 2111.
Sun, Z *et al. Chem. Rev.* **2018**, *118*, 614.

Cascade use of Biomaterials

Cascade of Value:



❶ log
❷ large dimensions solid or engineered timber assortments
❸ strand-/particle-based composites,
❹ fibre-based composites,
❺ chemicals,
❻ energy,

① resource extraction
② first life cycle
③ second life cycle
④ chemicals processing
⑤ energy generatio

Sandak, A., Sandak, J., Brzezicki, M., Kutnar, A. (**2019**). Biomaterials for Building Skins. In: Bio-based Building Skin. Environmental Footprints and Eco-design of Products and Processes. Springer.
https://doi.org/10.1007/978-981-13-3747-5_2
Rivela B, Hospido A, Moreira T *et al*. Life cycle inventory of particleboard: a case study in the wood sector. Int J Life Cycle Assess, **2006**, *11*(2),:106–113.

Processing Technologies for Biobased Building Residuals

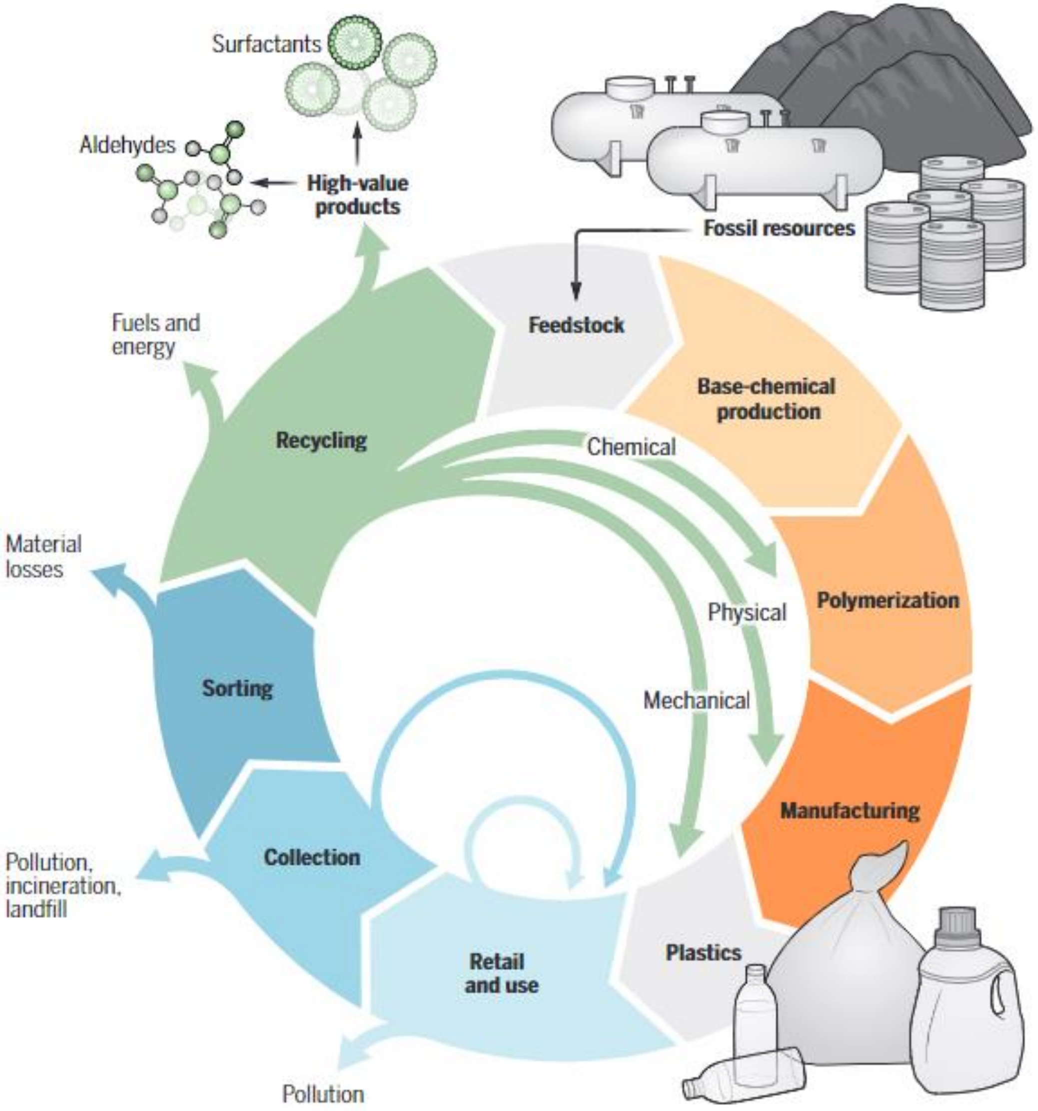
Cascade of Value:

Processing technology	Feedstock flexibility	Conversion efficiency	Market value of product
Combustion	High	Low	Low
Digestion	Low	Medium	Medium
Fermentation	Low	Medium	High
Pyrolysis	High	Medium	Medium
Gasification	Medium	Medium	Medium
Platform molecules	Medium	Medium	High
Liquefaction	Medium	Low	High
Composites manufacturing	High	High	High
Animal bedding	High	Medium	Low
Pelletizing	High	High	High
Insects conversion	Medium	Medium	High
Fungal conversion	Medium	Medium	High

Sandak, A., Sandak, J., Brzezicki, M., Kutnar, A. (**2019**). Biomaterials for Building Skins. In: Bio-based Building Skin. Environmental Footprints and Eco-design of Products and Processes. Springer.
https://doi.org/10.1007/978-981-13-3747-5_2

From Plastics

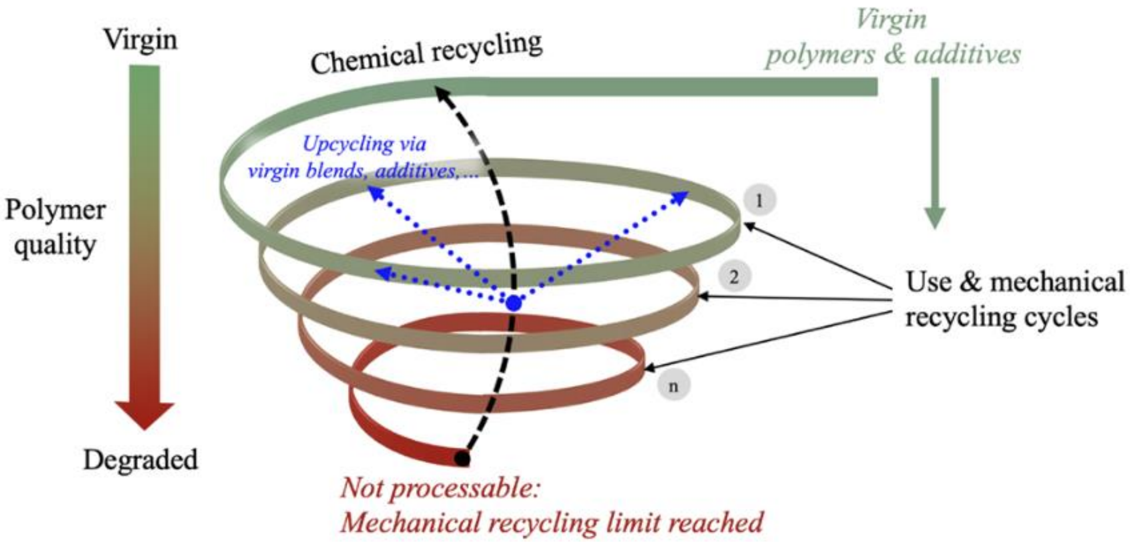
High Value Chemicals:



Van Geem, K. M. *Science* **2023**, Vol 381, Issue 6658, 607-608.
DOI: 10.1126/science.adj2807

From Plastics: Spirality?

High Value Chemicals:

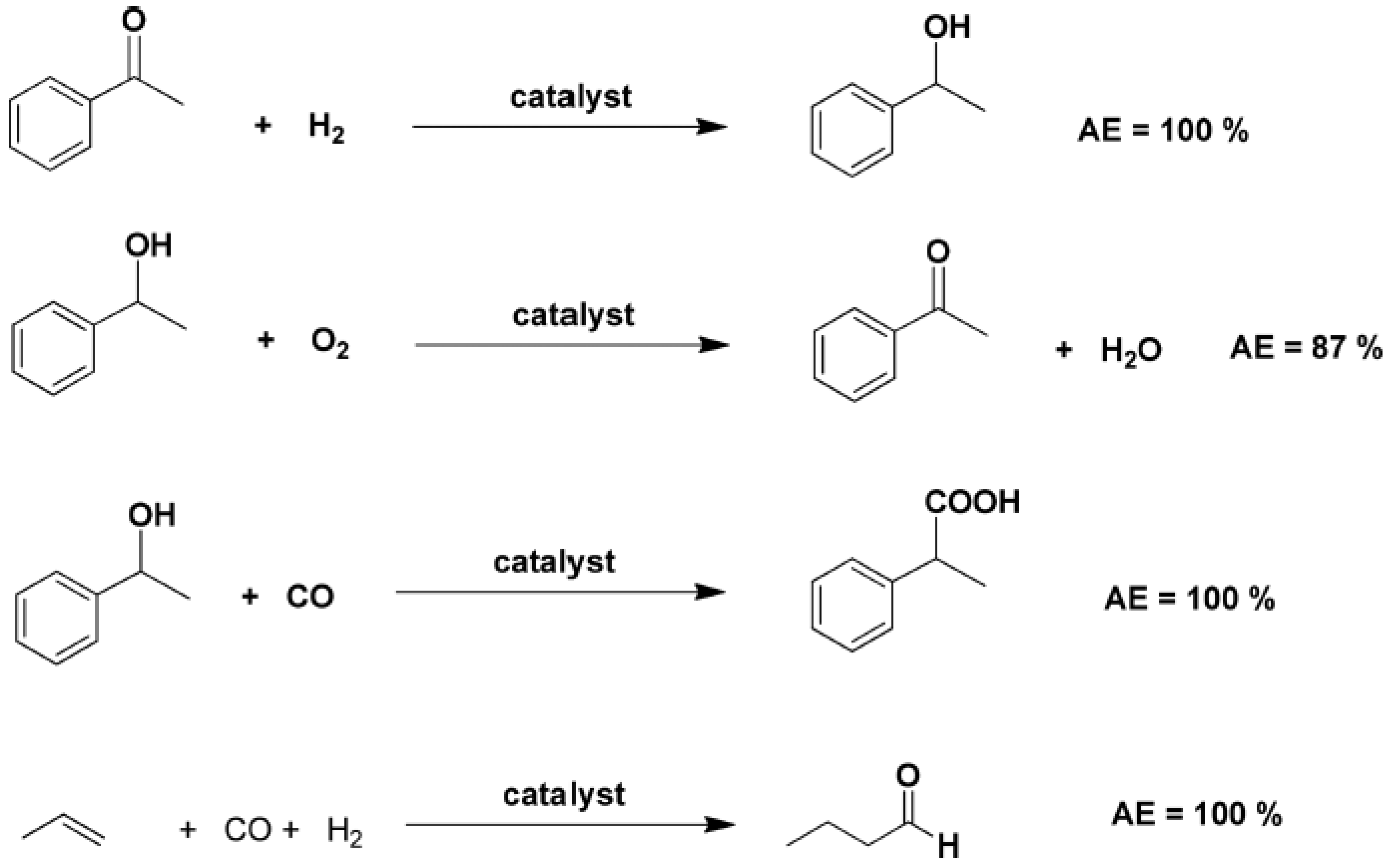


JACS, **2025**,
https://doi.org/10.1021/jacs.5c05454

Chemical Catalysis

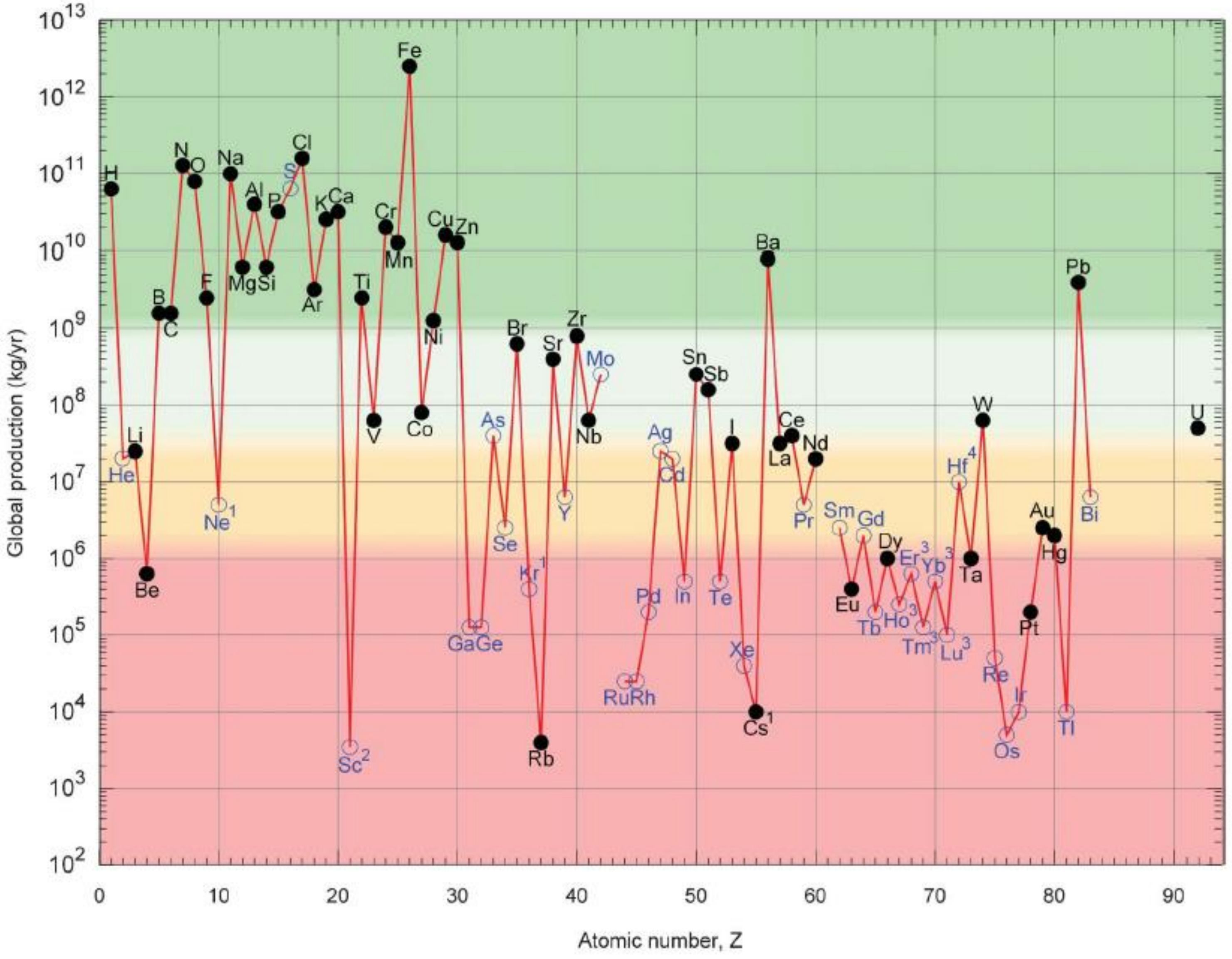
Chemical Catalysis:

Pros & Cons
Metrics?
Issues?



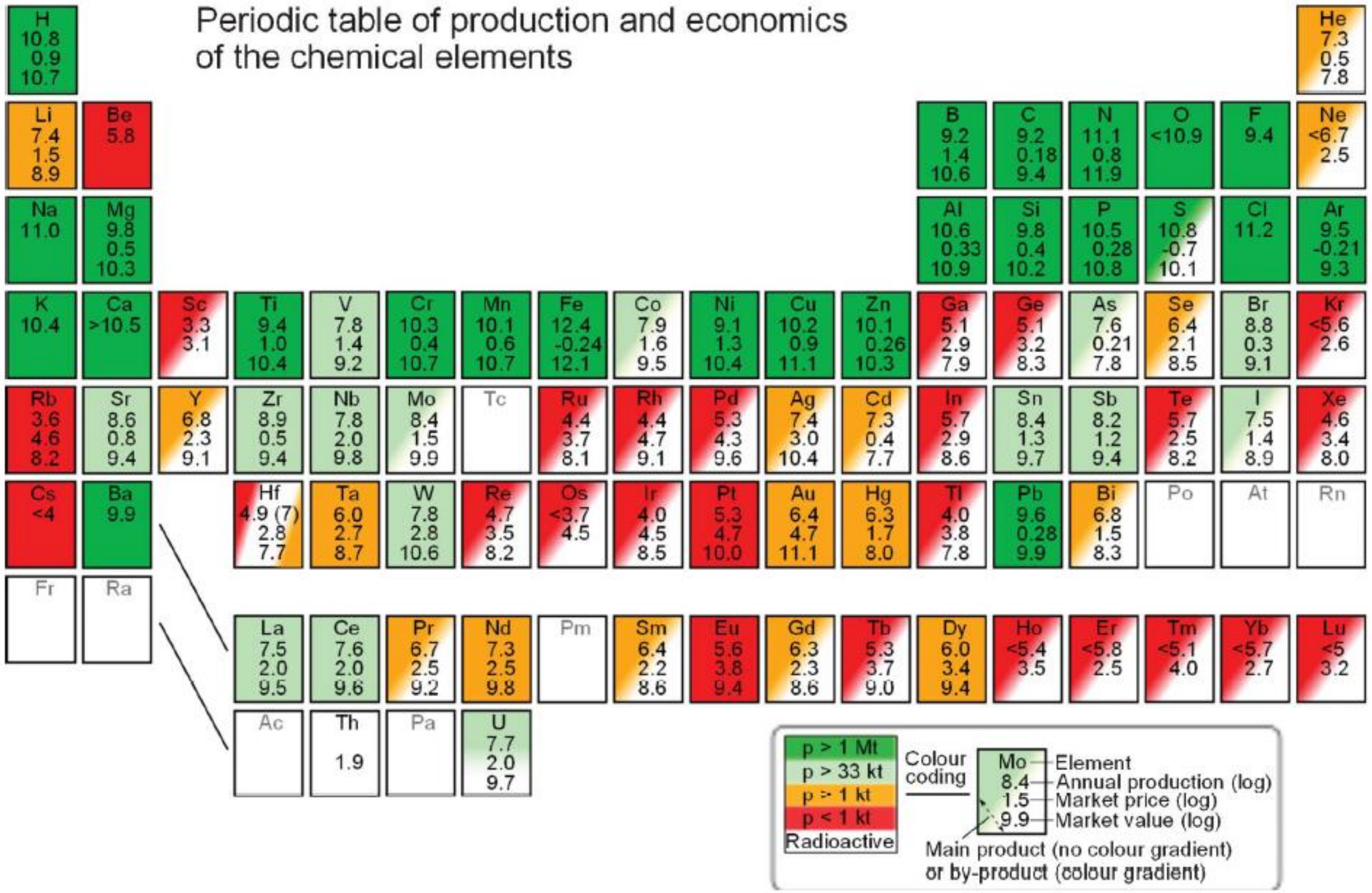
Sheldon, R. A. *ACS Sustainable Chem. Eng*. **2018**, *6*, 32.

Chemical Catalysis



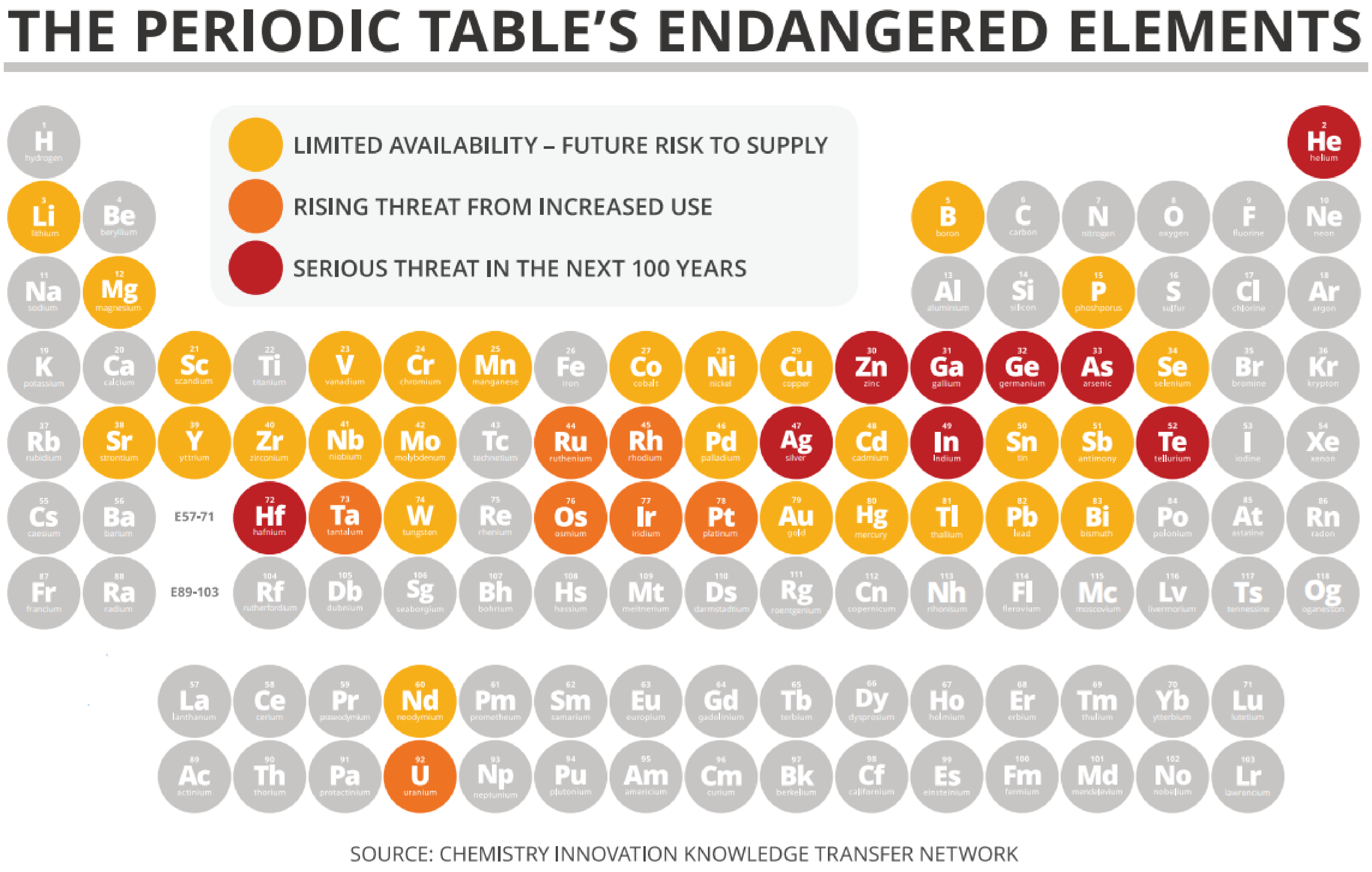
Vesborg, P. C. K.; Jaramillo, T. F. *RSC Adv*., **2012**, *2*, 7933.

Chemical Catalysis



Vesborg, P. C. K.; Jaramillo, T. F. *RSC Adv*., **2012**, *2*, 7933.

Chemical Catalysis



https://www.acs.org/greenchemistry/research-innovation/endangered-elements.html

Catalysis

Chemical Catalysis:

Synthesis of Ligands or Metallic Precursors? Green ? Sustainable?

From a sustainability, systems, and life cycle perspective:

- Type and chemical nature of the catalyst matters.
- Where and how the metals, the reagents, chemicals, and solvents are sourced.
- The reaction conditions required for the catalysis to proceed.
- The disposition of these components in use disposal.

No clear metric available.
But the impact of the catalysz during process development could be evaluated via: E-Factor, PMI, etc.

Hazardeous Score

Hazardeous Reactants & Reagents:

Hazard vs risk ?

A hazard is any source of potential damage, harm or adverse health effects on something or someone
Risk is the chance or probability that a person will be harmed or experience an adverse health effect if exposed to a hazard

Chemists have to recognize functional groups and structural motifs that lead to hazardous properties (environmental, safety, and human health) in order to avoid them.

Chemists should recognize and pursue ways to change the chemistry system to one that has minimal adverse impacts and promotes a more sustainable planet.

https://www.ccohs.ca/oshanswers/hsprograms/hazard/hazard_risk.html

Hazardeous Score

Hazardeous Reactants & Reagents:

Fire/Explosion:

- Oxidizer
- Combustible

Reaction/Decomposition:

- Thermal Stability:
- Incompatibility
- Exothermic Reaction

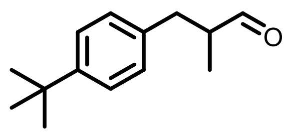
Toxicity Acute or Chronic:

- Carcinogenicity
- Mutagenicity
- Reproductive Tox.
- Sensitization
- Other

And finally what about the final ingredient?
And by-product during the synthesis?

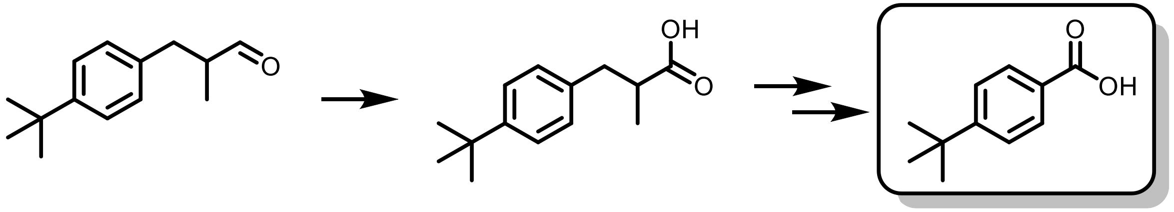
Hazardeous Score

Example from Perfumery Industry: Lyral Case Study



Lyral, widely used perfumery ingredient
Lilly-of-the-valley smell

Toxicity of Metabolized Lyral:



Further link to CoA and as a consequence: impair male reproduction.

Laue, H. *et al. Toxicological Sciences*, **2017**, *160(2)*, 244.

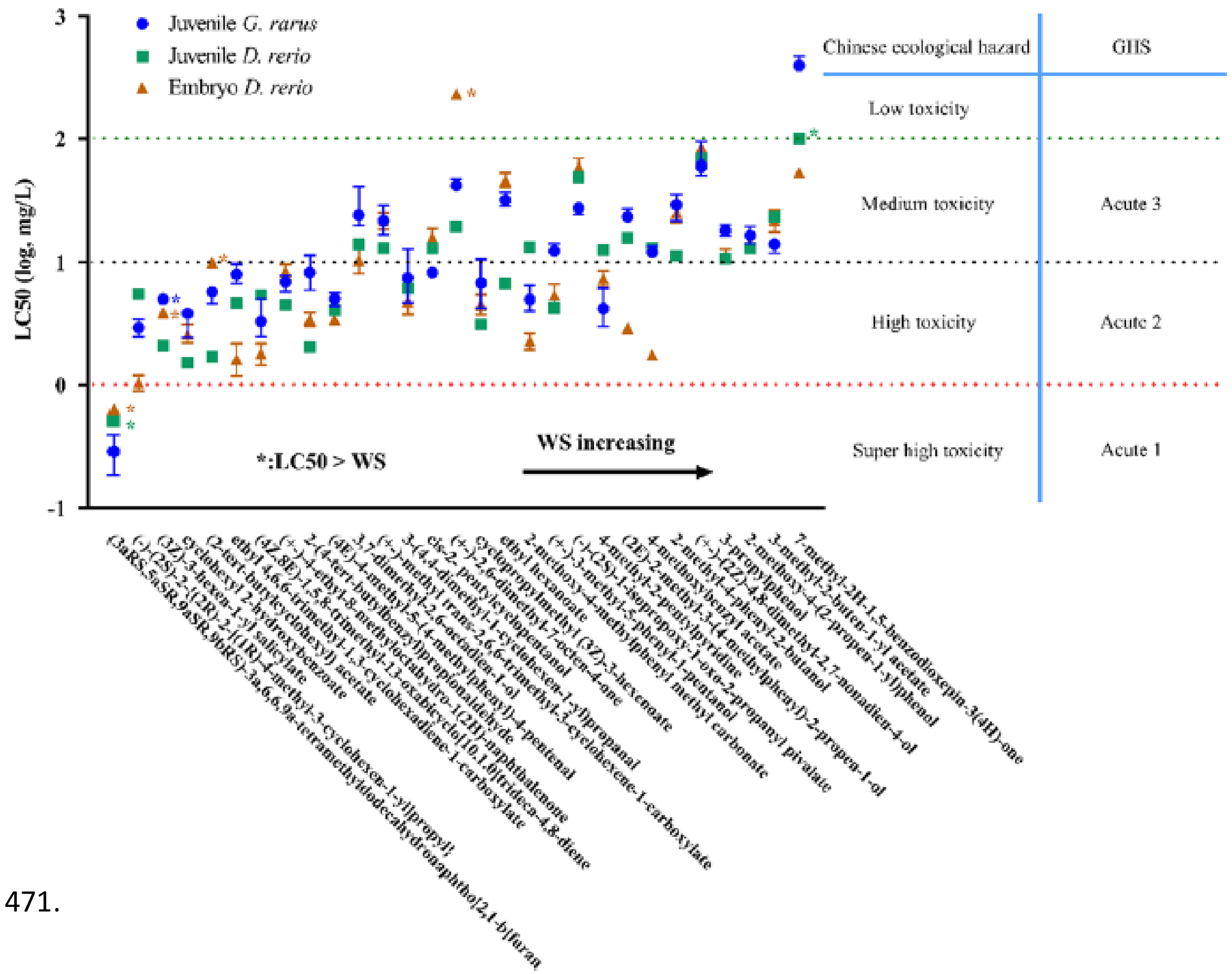
Hazardeous Score

Example from Perfumery Industry:

Toxicity of perfumery Ingredients on 2 different Zebrafish

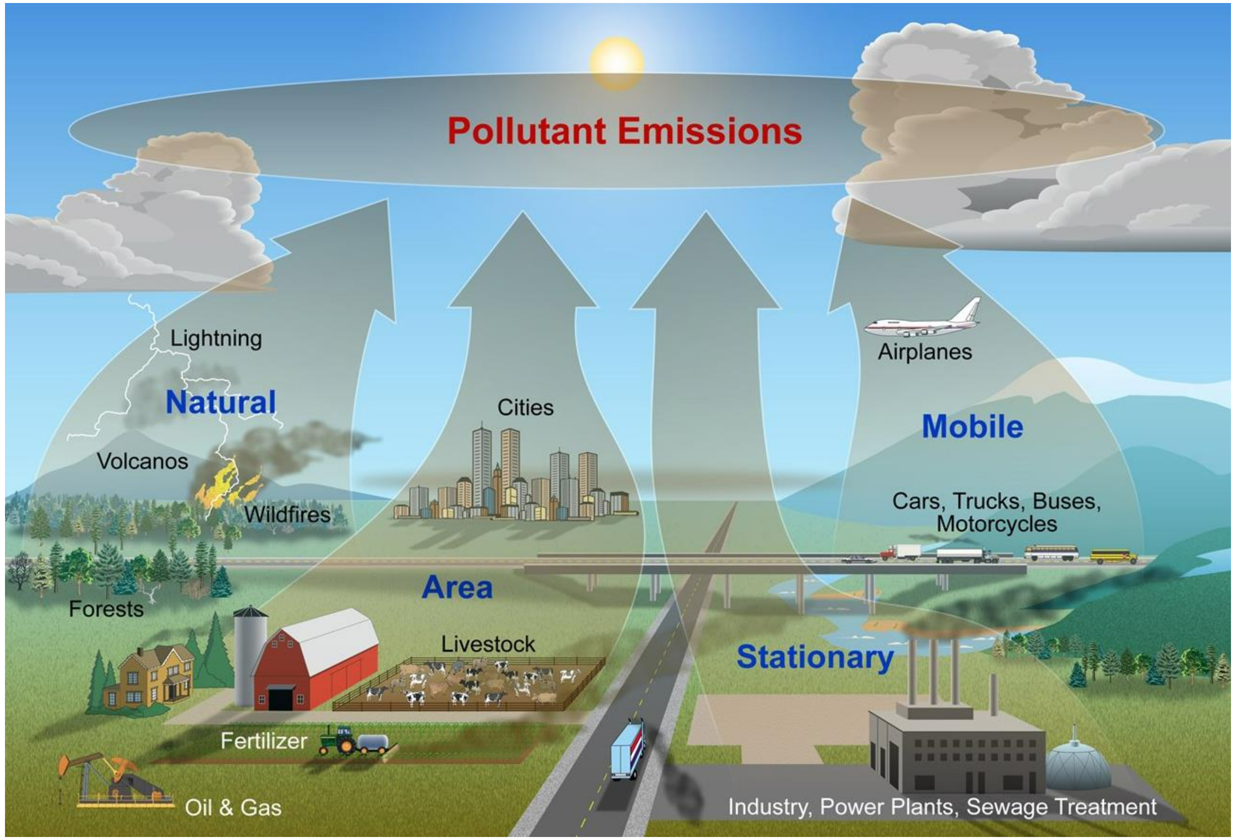
29 ingredients: different physical properties, structures

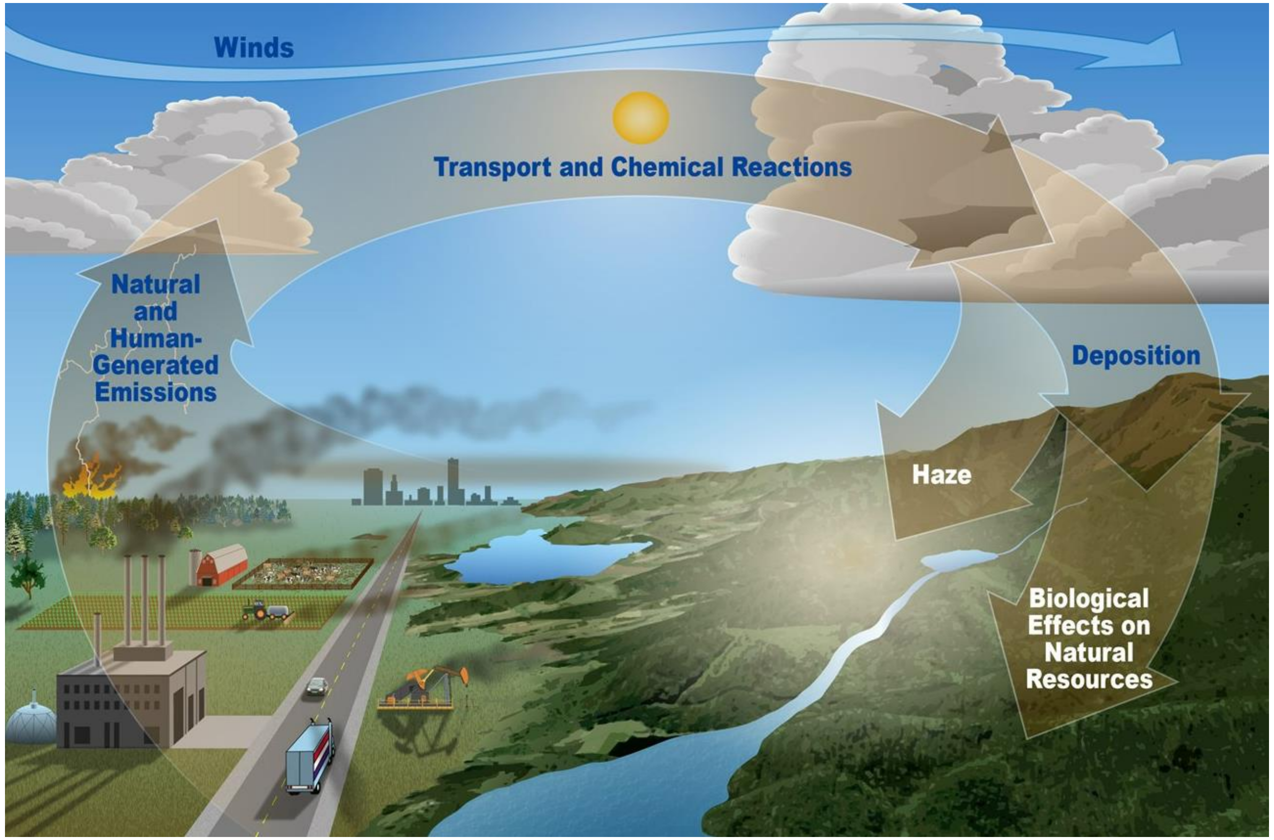
Based on Verhaar categories



Zhou, Z. *et al. Environmental Toxicology and Chemistry*, **2022**, *41(9)*, 2305.
Verhaar, H. J. *et al.* Classifying environmental pollutants. *Chemosphere*, **1992**, *25*, 471.

Biodegradation/(Bio)-Accumulation Score

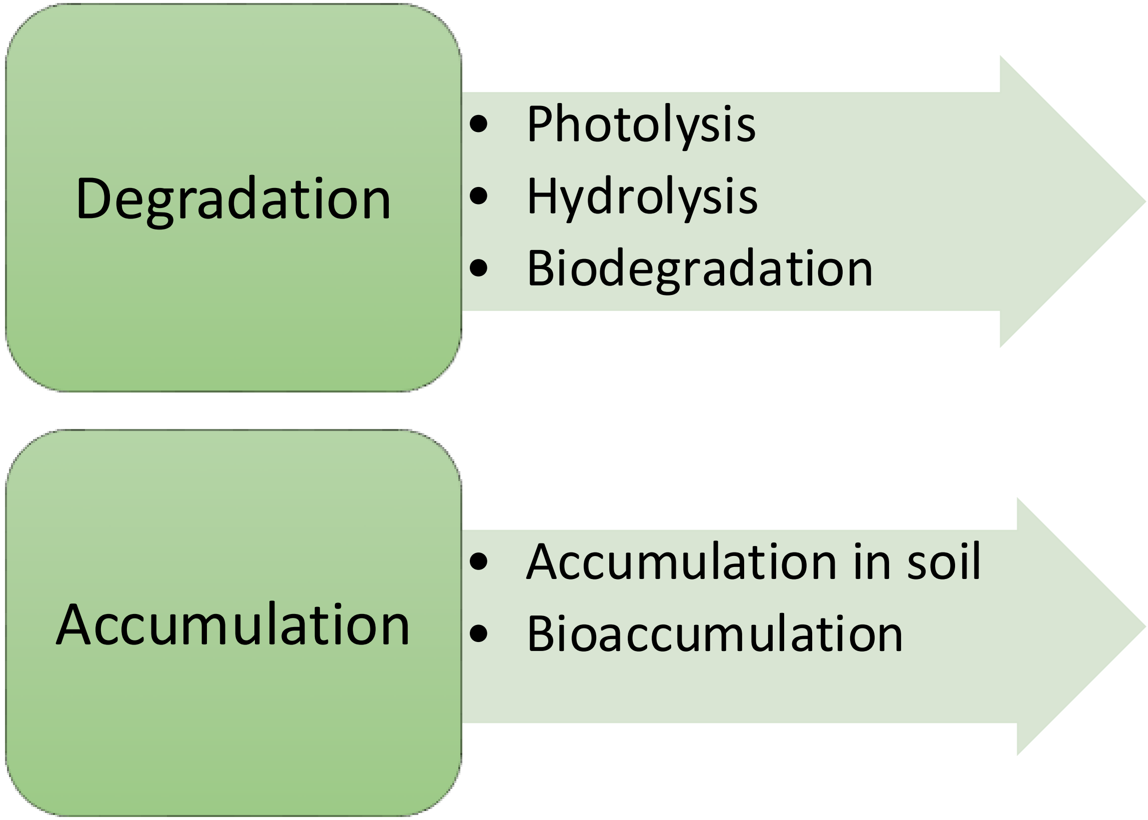




https://www.nps.gov/subjects/air/sources.htm

Biodegradation/(Bio)-Accumulation Score

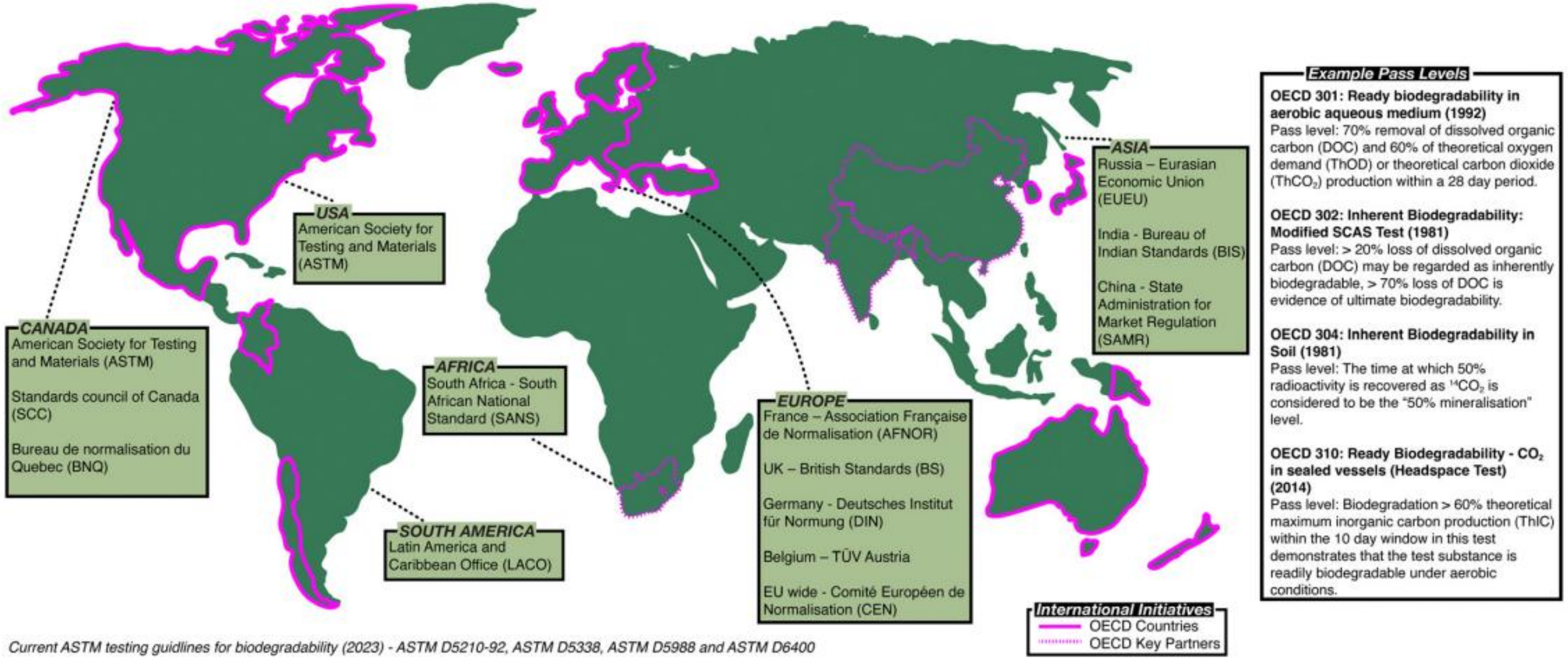
Biodegradation/(Bio)-Accumulation Score



Koller, G. *et al. Assessing Safety, Health, and Environmental Impact Early during Process Development*
Ind. Eng. Chem. Res. **2000**, *39*, 960.

Biodegradation/(Bio)-Accumulation Score

The global regulatory landscape for assessment of biodegradation

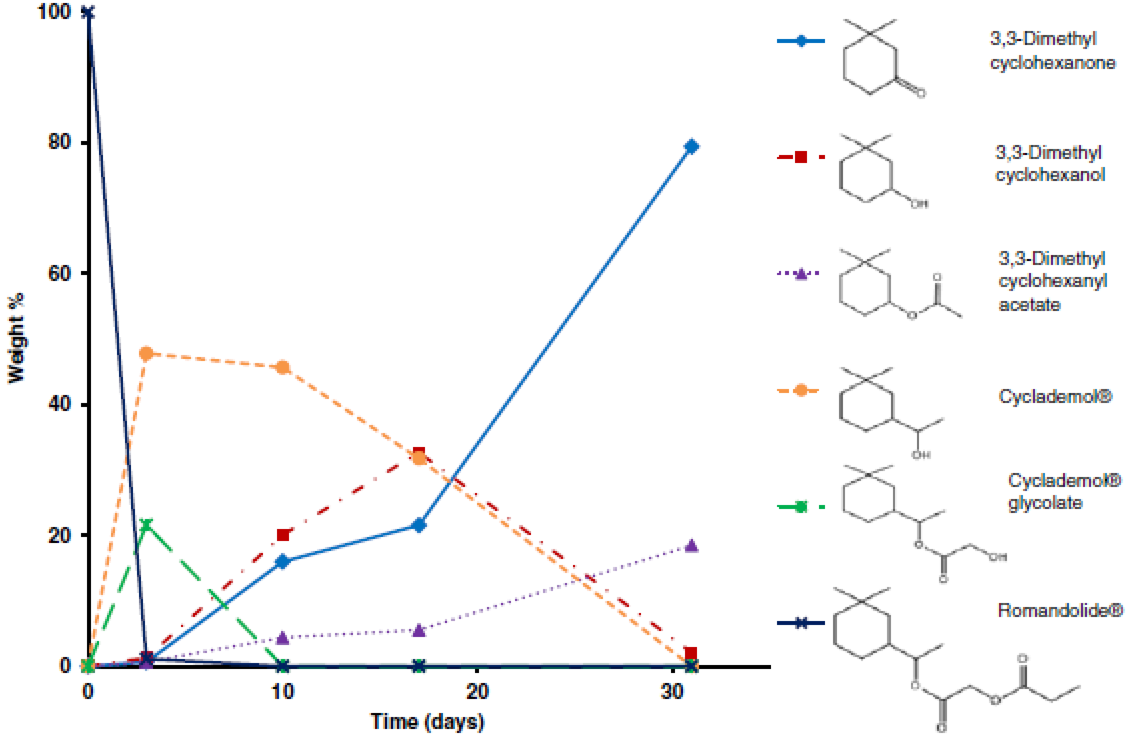


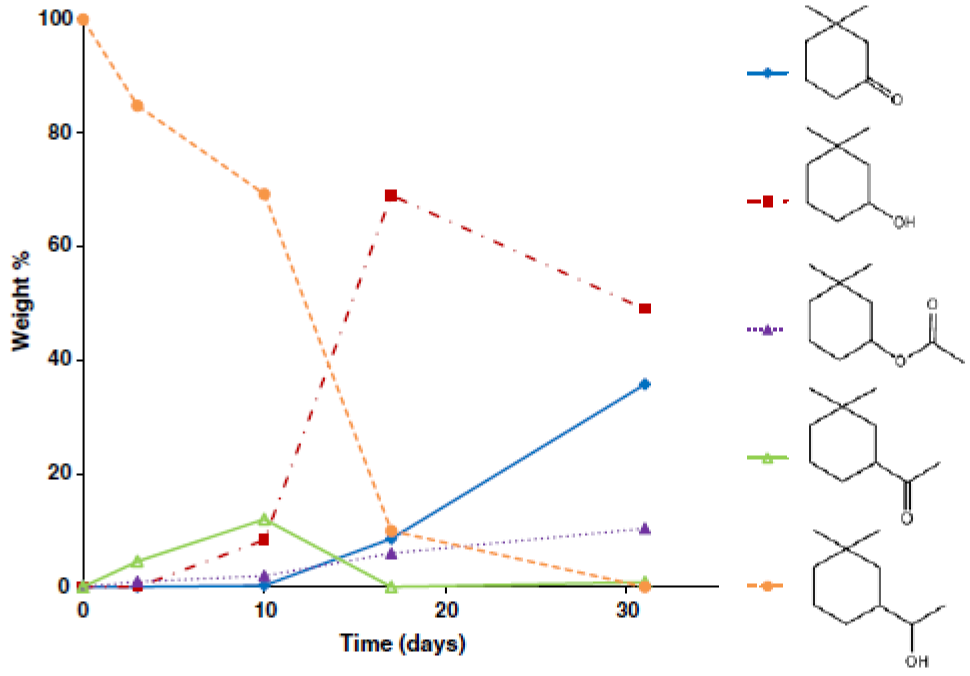
Chem. Soc Rev. **2023**, DOI: 10.1039/d3cs00556a

Biodegradation/Bioaccumulation Score

Example from Perfumery Industry:

Acyclic musk Romandolide in activated sludge; OECD Screening tests



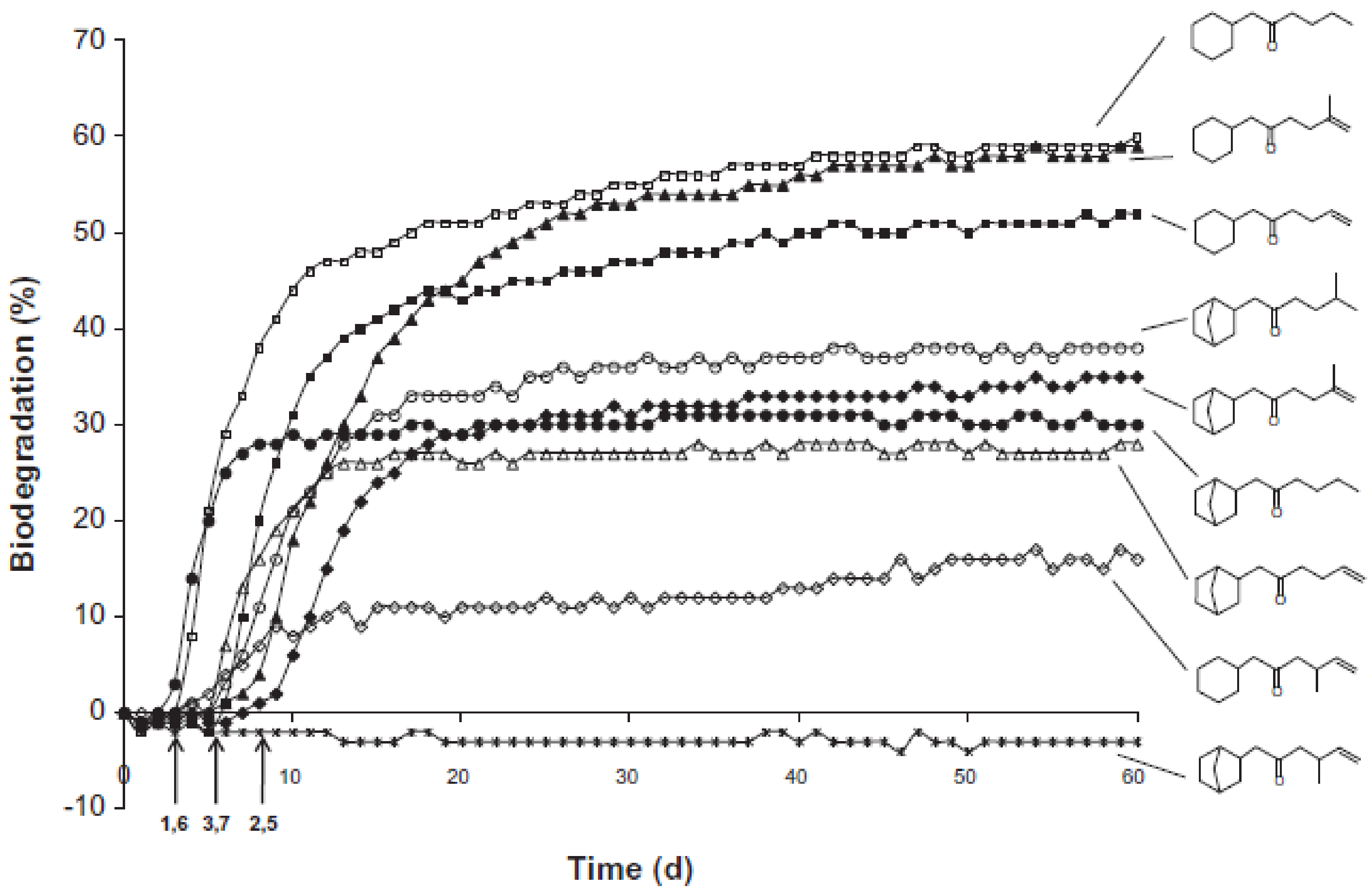


Seyfried, M *et al. Environ Sci Pollut Res* **2013**, DOI 10.1007/s11356-013-2347-9

Biodegradation/Bioaccumulation Score

Example from Perfumery Industry:

Persistence assessment of cyclohexyl- and norbornyl-derived ketones; OECD Screening tests

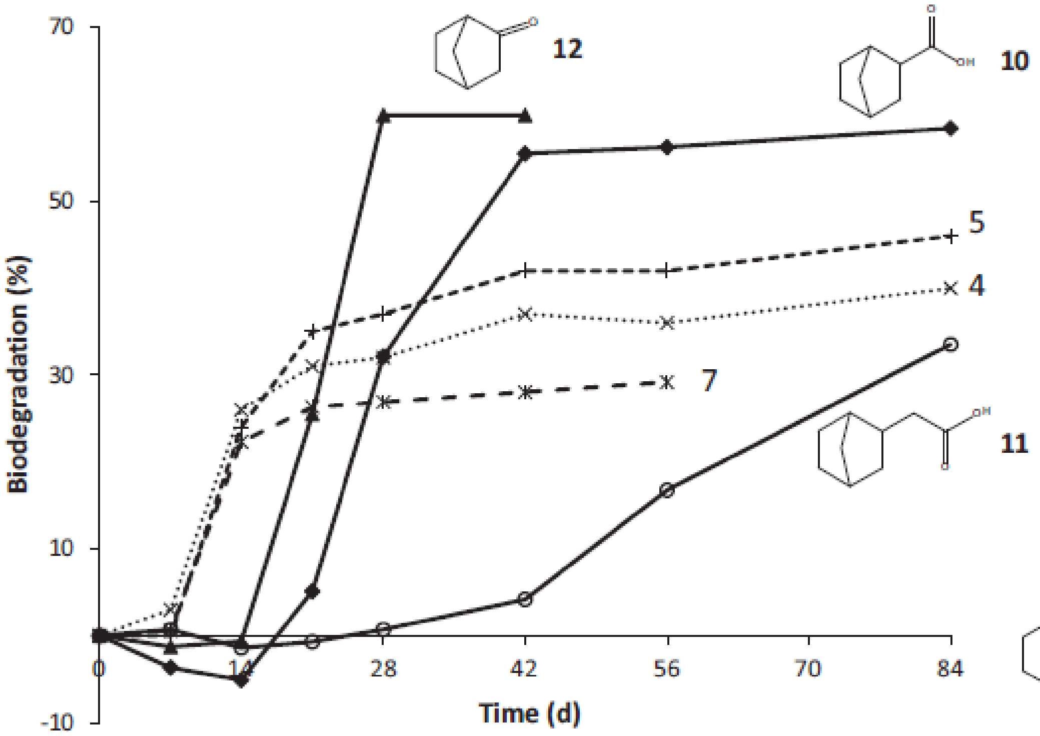


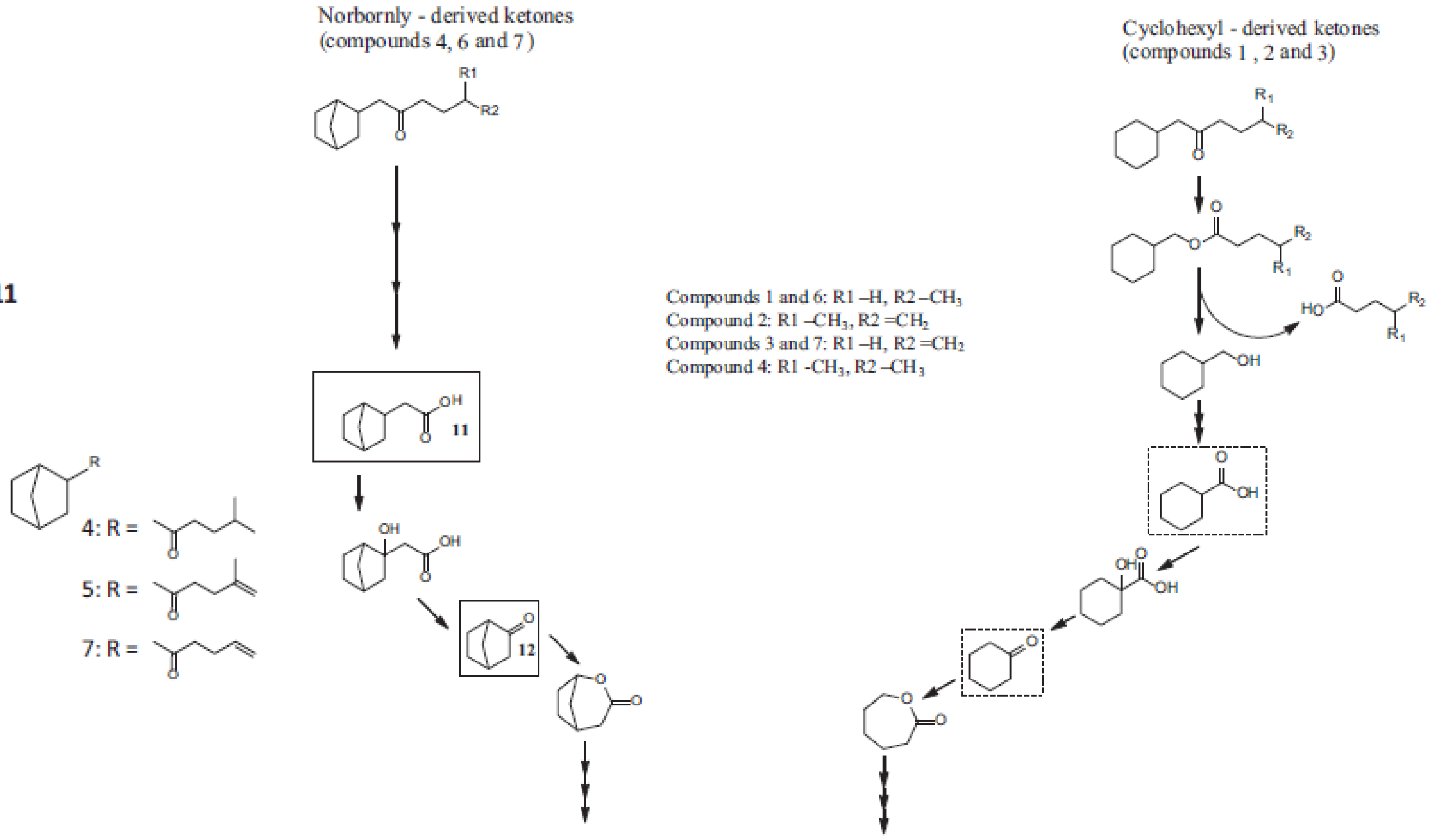
M. Seyfried *et al. Chemosphere* **2015**, *131*, 63.

Biodegradation/Bioaccumulation Score

Example from Perfumery Industry:

Persistence assessment of cyclohexyl- and norbornyl-derived ketones; OECD Screening tests

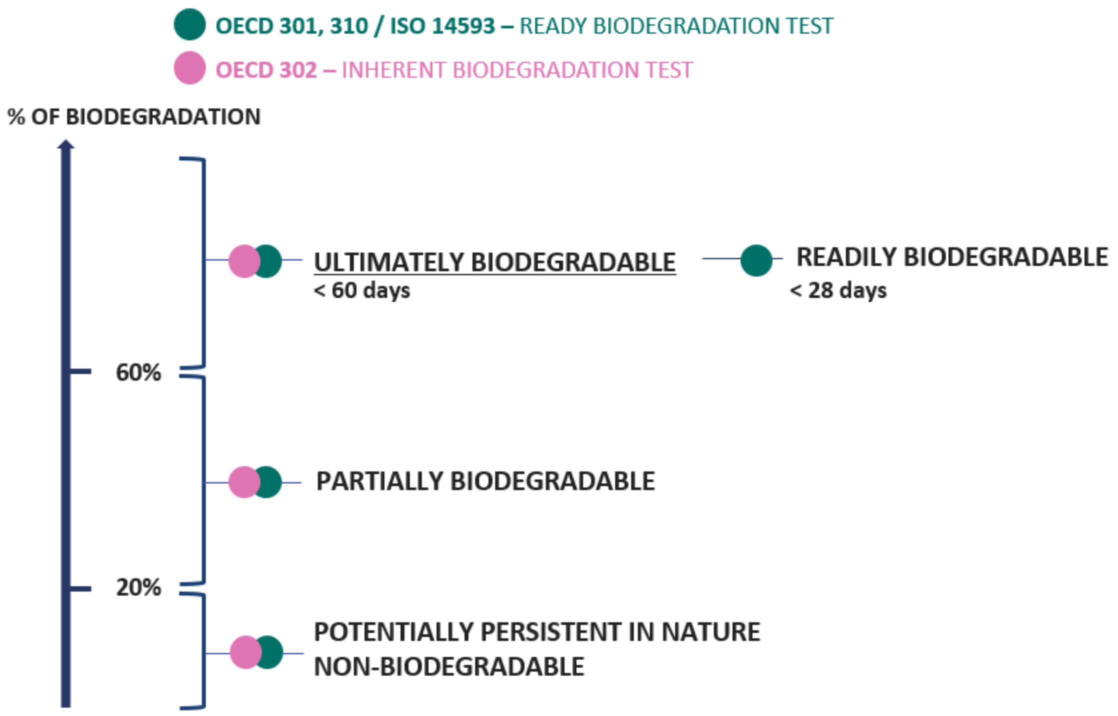




M. Seyfried *et al. Chemosphere* **2015**, *131*, 63.

Biodegradation/Bioaccumulation Score

Example from Perfumery Industry:
Biodegradation



https://www.oecd.org/chemicalsafety/

Energy Metrics

Energy

2 major cases:

- Commodity chemicals, in contrast, energy consumption plays a prominent rôle and could be perfectly calculated
- Multipurpose production facilities, energy usage is often not allocated to particular processes.

Curzons, A. D. *et al.* Green Chemistry, 2001, 3, 1.
https://www.oecd.org/innovation/green/toolkit

Energy Metrics

Energy

Energy Intensity = (Energy consumed in the production process + energy consumed in overhead)/kg of Material Produced

Energy

$$\frac{\text{Total process energy (MJ)}}{\text{Mass of product (kg)}} \qquad \text{MJ/kg}$$

M. Bernstein, K. Fonkych, S. Loeb, D. Loughran, State-Level Changes in Energy Intensity and Their National Implications, RAND, Santa Monica, **2003**.
https://www.rand.org/pubs/monograph_reports/MR1616.html

Energy Metrics

Energy for solvent recycling

Energy

$$\frac{\text{Total solvent recovery energy (MJ)}}{\text{Mass of product (kg)}} \qquad \text{MJ/kg}$$

Alan D. Curzons *et al.* *Green Chem.* **2001**, *3*, 1.

Energy Metrics

Energy

Production of Energy produces CO_2....as a waste often negliged during the E-Factor calculation

Not in E-factor: heating, cooling, stirring, pumping, etc.

$$E^{+} = \frac{\sum m(wastes)}{m(products)}\frac{kg}{kg} + \frac{W \times CI}{m(product)}\left[\frac{kWh \times \frac{kg(CO_2)}{kWh}}{kg}\right]$$

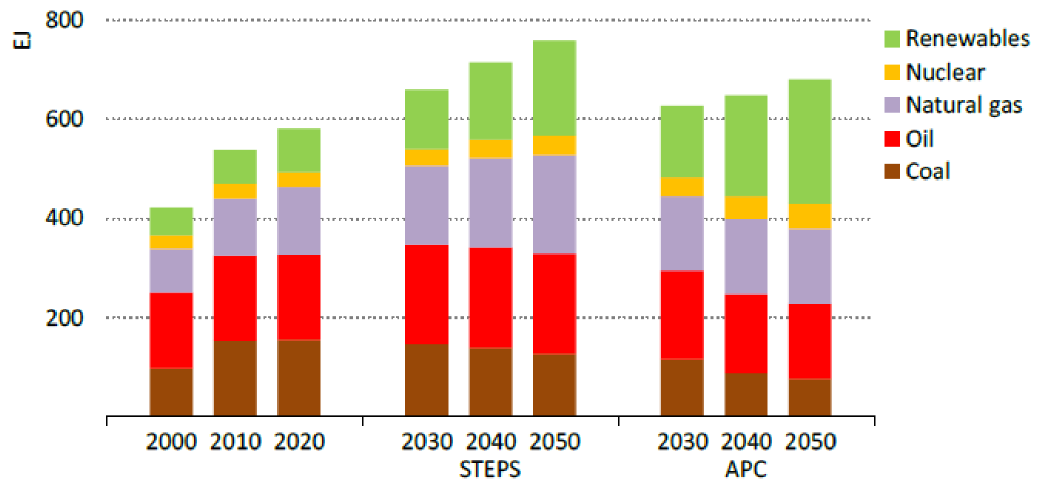
W = electrical power used
CI = carbon intensity, i.e. the local average CO_2 emissions caused for the generation of electricity.

Tieves, F. *et al. Tetrahedron* **2019**, *75*, 1311.

But the world does not stand still

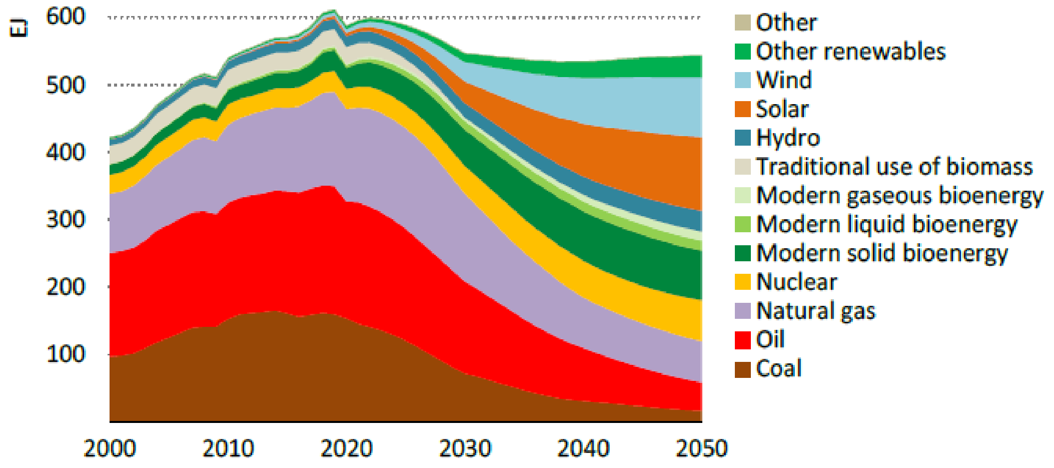
The energy transition will lead to shifts in energy sources ⇨ towards more renewable energy sources.

Figure 1.12 ▹ Total energy supply by source in STEPS and APC



Announced net zero pledges lift renewables in the APC from 12% of total energy supply in 2020 to 35% in 2050, mainly at the expense of coal and oil

Figure 2.5 ▹ Total energy supply in the NZE



Renewables and nuclear power displace most fossil fuel use in the NZE, and the share of fossil fuels falls from 80% in 2020 to just over 20% in 2050

Will that make a difference to Carbon Footprints?
How to implement that transition into LCA-models?

IEA report "Net Zero by 2050, A Roadmap for the Global Energy Sector" 2021.

Natural Extracts

Nagoya Protocole:

Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity

Adopted in 2010
Entered in force in 2014
In 2022, ratified by 137 states

Benefit-sharing obligations
Compliance obligations

https://www.cbd.int/abs/doc/protocol/nagoya-protocol-fr.pdf

Natural Extracts

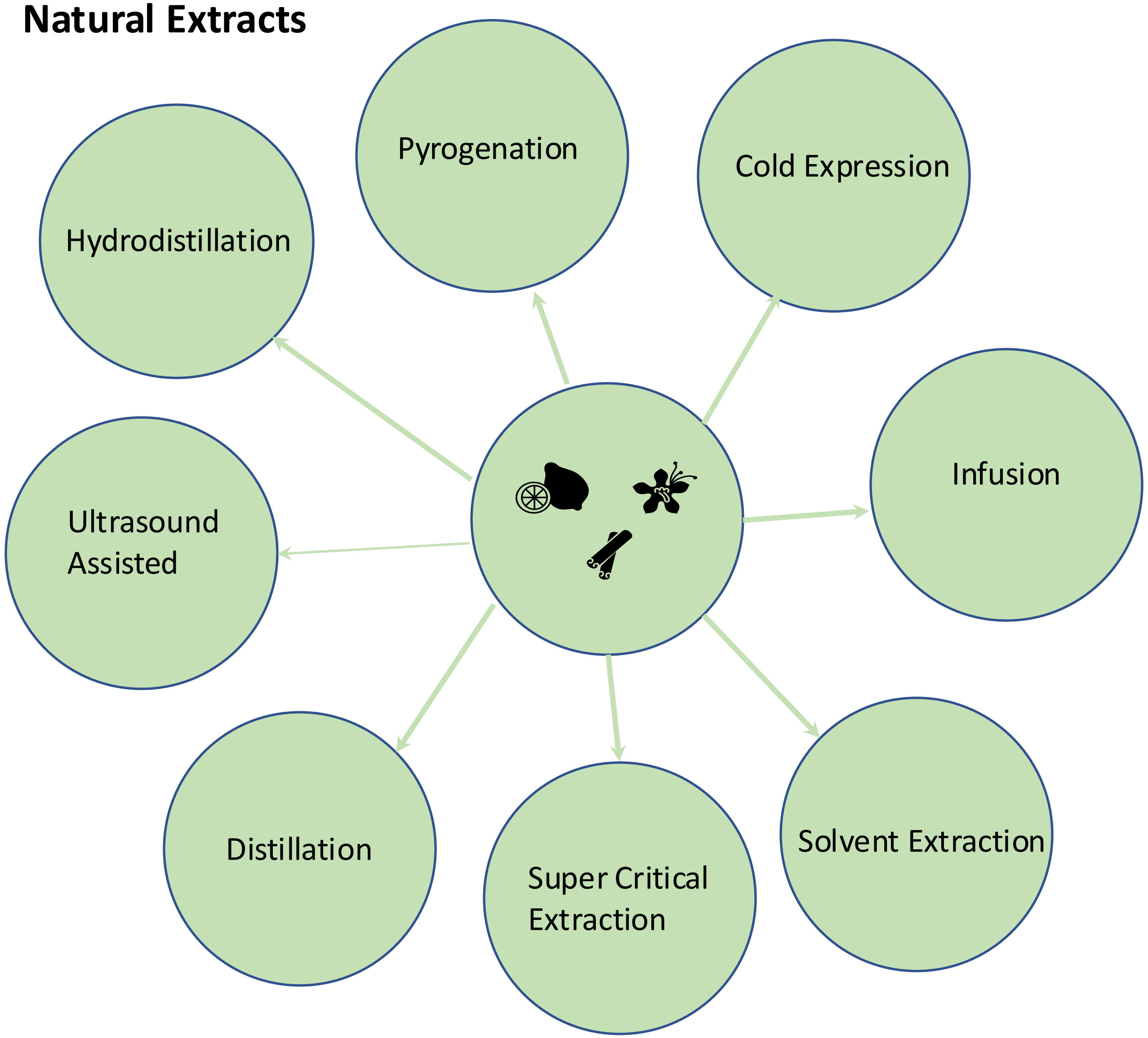
Natural Extracts

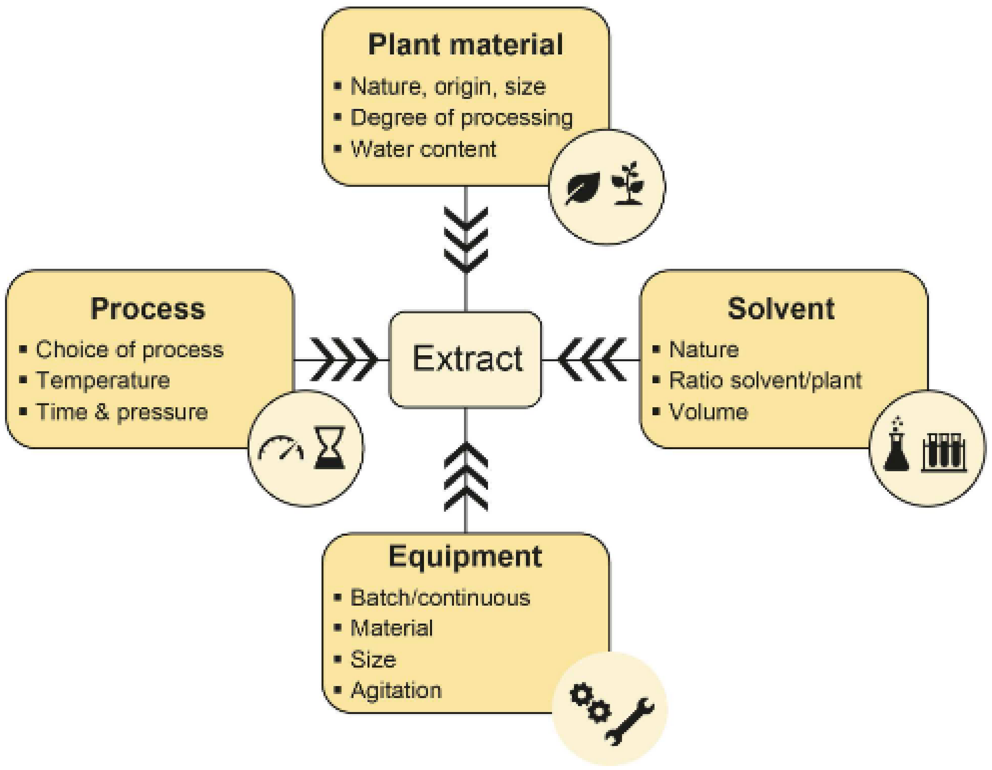
Category	Agrochemicals	Cosmetics	Aroma, Flavours and Nutrition	Pharma
Market volume	1 Billion USD	200 Billion USD	10 Billion USD	107 Billion USD (forecast 2017) [21]
Market growth	Double digit annual growth rate	Double digit annual growth rate	Double digit annual growth rate Market for nutrition additives decreases Market for aromas grows	Double digit annual growth rate Decline in prescription market Growth in over-the-counter market
Challenges	Market dominated by SMEs as well as global players Small volume/low cost products bulk High cost/low volume niche products	Significant amount of products with natural claims but up to 75% synthetic ingredients; No uniform and binding standards for natural, fair-trade, organic labels	Low cost products (in the order of 1–10 €/kg) Many products with small volumes (100–1000 kg/a)	Most products are OTC Only few blockbusters Restrictive regulatory hamstringed R&D
Medium-term research demands	Efficient total process design for SMEs; Integrate process intensification Methods for SMEs and scale-up of infrastructure to fully integrated manufacturers; Energy efficient and low waste processes for decentralised utilization of natural resources [21,22] *	Efficient ways of finding new natural ingredients [23,24]; * Ensuring sustainability of supply	Apply and adopt more often $scCO_2$, bio-based solvents *, PHWE Biomass valorization, e.g., carrot, broccoli, artichoke etc. do have 30–80% herbal raw material waste	Speed up of development of herbal raw cell fermentation by omics [25] * Process Analytical Technology for inline-analysis of extraction processes; Parametric defined release at manufacturing of herbal raw extracts; * Homogeneity at production of extracts in large-scale Lyophilisation instead of vacuum-belt drying; Fresh herbal raws instead of dried raw material; HGACP instead of GMP on field incl. extraction media and pomace to be deposited on field again
Long-term research demands	Development of new products	Shift from wild collection to greenhouse or field cultivation in Europe; Energy efficient and low waste processes for decentralised utilization of natural resources [21,22]	Energy efficient and low waste processes for decentralised utilization of natural resources [21,22]	Determination of distribution behaviour of herbal raw ingredients in "single pot model" with herbal raw cell membranes and a gastrointestinal membrane for fast prediction of bioavailable components; Efficacy studies for new herbal raws and products which enable IP protection to cover the costs via patents on the new processes

Uhlenbrock, L. *et al. Processes* **2018**, *6*, 177.

Natural Extracts

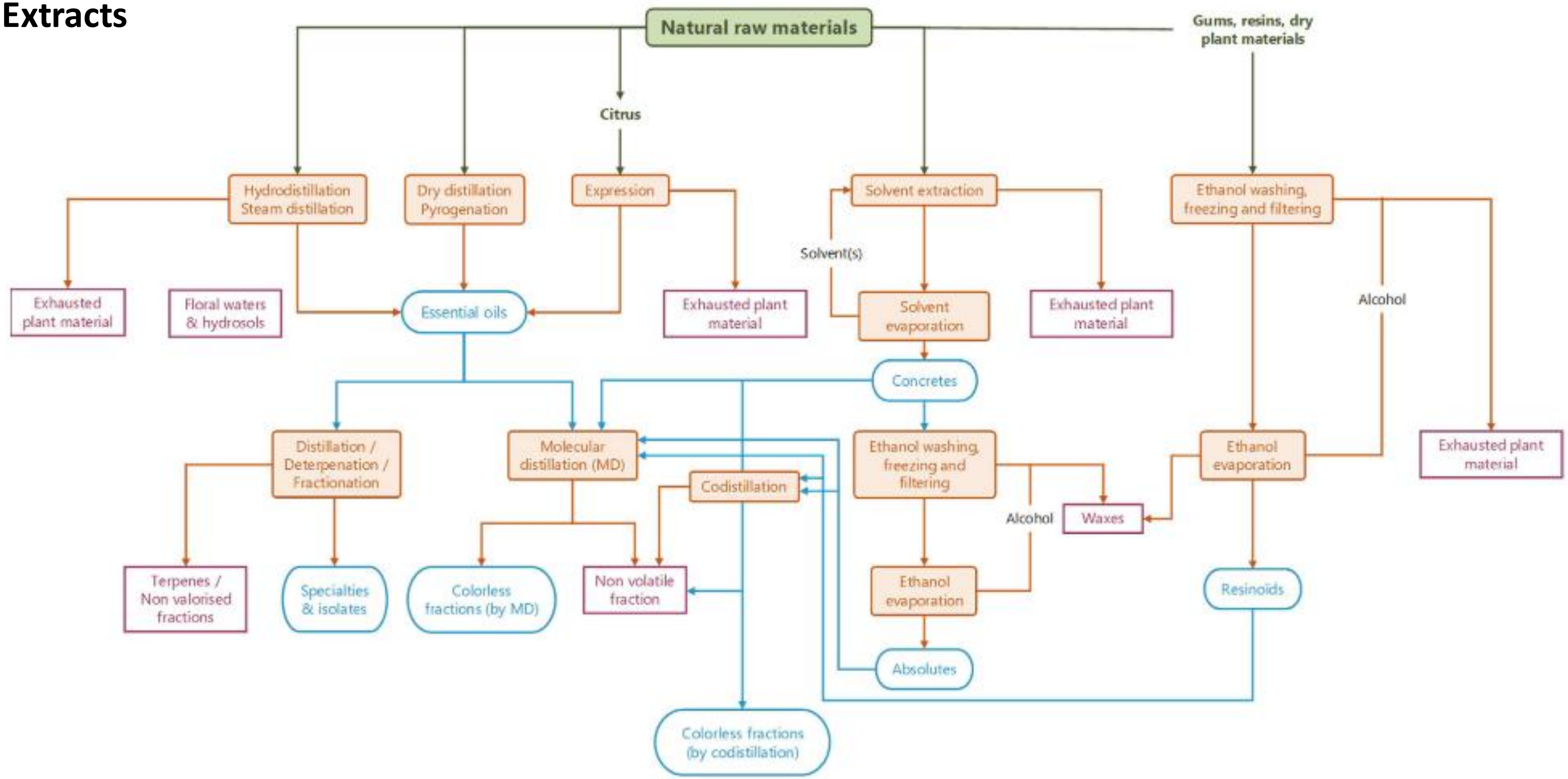
Natural Extracts





Natural Extracts

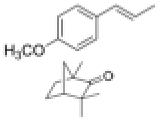
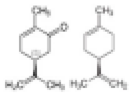
Natural Extracts



Burger, P. *et al. Chem. Biodiversity* **2019**, *16*, e1900424.

Natural Extracts

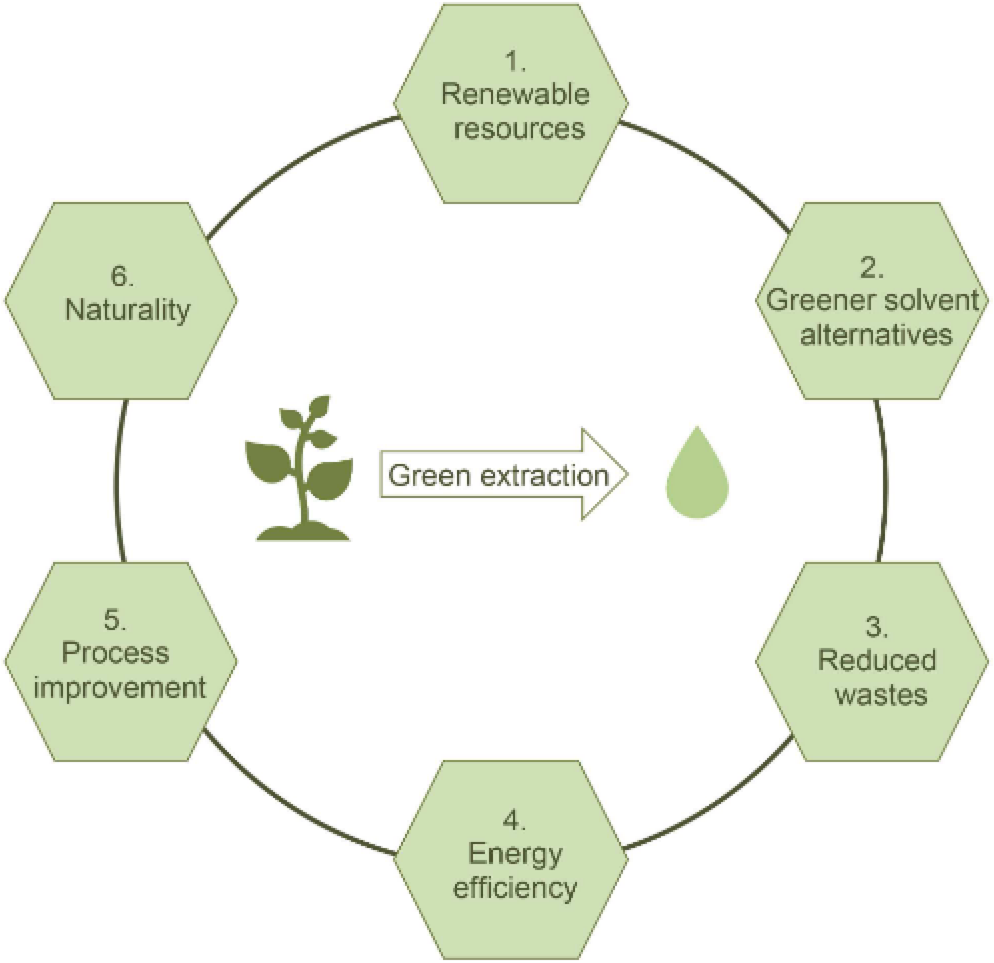
Natural Extracts

Category	*Foeniculum vulgare* L. Mill.	*Carum carvi* L.
Use	Aroma/fragrance	Aroma/fragrance
Target component	Anethole (5.3%), Fenchone (2.9%) essential oil (~8% w)	Carvone, Limonene essential oil (~2% w)
Molecular structure and weight		
	148.2/152.23 Da	150.22 Da
Side component	Estragole (0.2%)	
Molecular structure and weight		
	148.2 Da	
Location	Fruit Oil channels	Fruit Oil channels
Solvent	Ethanol [60]	

Burger, P. *et al. Chem. Biodiversity* **2019**, *16*, e1900424.

Natural Extracts

Natural Extracts



Burger, P. *et al. Chem. Biodiversity* **2019**, *16*, e1900424.

Natural Extracts

Natural Extracts

Energy Intensity?

Land Impact & Societal Impact?

Extraction Yield? Recycling of Solvent or «Green» Solvent?

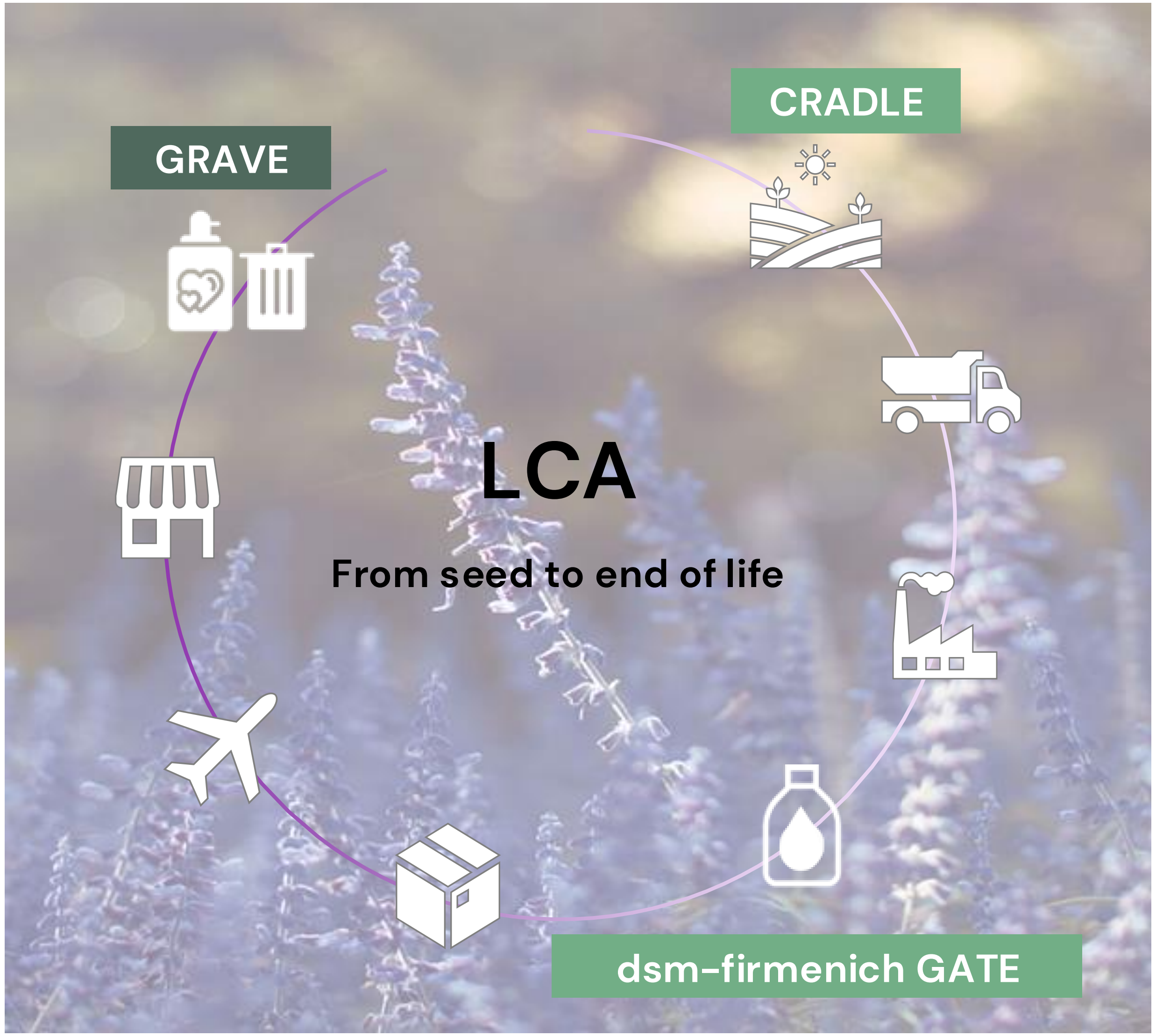
Ethical questions & Problems

https://www.firmenich.com/ingredients/technology

Beyond Green Metrics & Sustainability Metrics

What's next?

Life cycle Analysis/Inventory
Carbon Footprint



https://eplca.jrc.ec.europa.eu/uploads/ILCD-Handbook-Recommendations-for-Life-Cycle-Impact-Assessment-in-the-European-context.pdf

Measure today To shape tomorrow

Precision through data

100% LCA Data on all ingredients in 2024

Global standards

Foster Carbon Emissions data access & exchange

Data-driven future

Track, inform & drive progress towards decarbonisation

LCA/LCI

Life cycle Analysis/Inventory Definition

LCA

Life-cycle assessment (LCA) is a procedure for quantifying the total environmental impact of a product or service across its entire lifetime. This multi-step process includes goal and scope definition, inventory analysis, impact assessment, and interpretation. LCAs are iterative by nature as the plausibility, quality, and completeness of pertinent information changes over time.

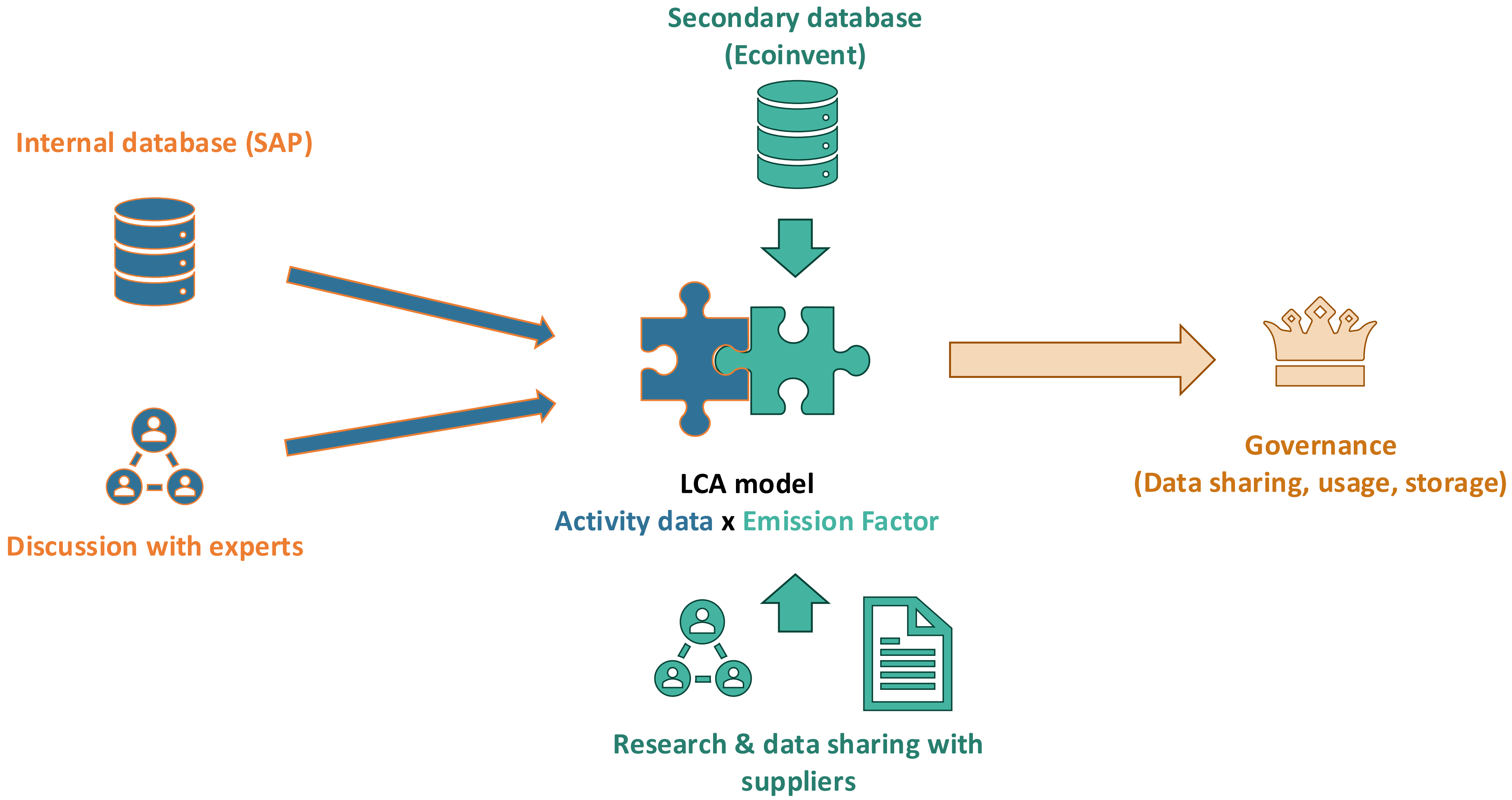
LCI

Life-cycle inventory (LCI) is the data-collection component of an LCA. Basically, an LCI endeavors to take an account of everything involved in the product or service. LCI considers the "system" at play by tracking all the inputs and outputs involved in making the product or service. The detailed accounting may include raw resources or materials, energy by type, water by source, and the various emissions to air, water, and/or land by substance. An LCI may be extremely complex, involving any number of individual unit processes contributing to relevant supply chains (e.g., the extraction of raw materials, various production processes, transportation, etc.) along with any/all constituent substances (for which there could be hundreds).

LCA is inherently uncertain, and communication of LCA results should therefore account for uncertainty.

Kleinekorte, J. *et al.* *Annu. Rev. Chem. Biomol. Eng.* **2020**. *11*:20.1–20.31

LCA data management: Activity data – Emission factor - Governance



Carbon Footprint: Order of magnitude

kg CO_2-eq / kg

0	5	10	20	50	100	1000	10000

0–5	5–10	10–20 (20)	50	100–1000	1000–10000
Acetone Ethanol Methanol Toluene CST	Pyridine Organo-phosphorous Vegetable oil	PDMS Special inorganic salt Medium complex organic chemicals	Complex organic chemicals Essential oil (wood, lavender, castor oil)	Natural extraction with low yield EO with specific sourcing Land use change	Extra pure natural extracts Precious metal catalyst (Pt, Pd)

1 kWh electricity
0,5 kg CO_2-eq (EU mix)
0,05 kg CO_2-eq (Solar PV)
20 smartphone charge/discharge

1 day emission for an avg Swiss
38 kg CO_2-eq / day

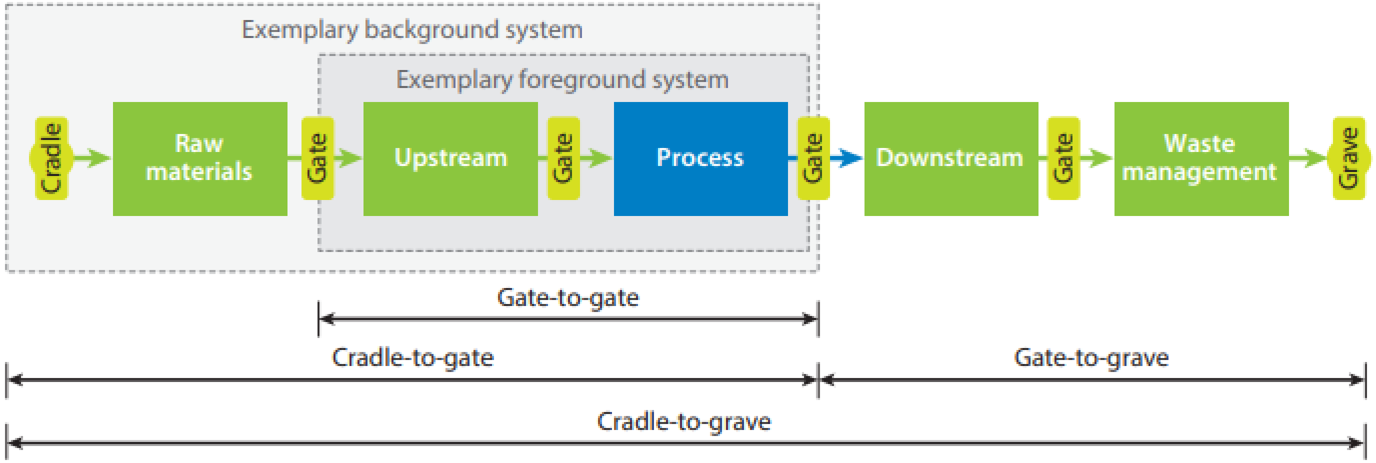
14t per year (scope 1/2/3)

Zürich – Auckland in Economy
3'700 kg CO_2-eq / travel

LCA/LCI

Boundary of the System:

Modular cradle-to-gate life cycle inventory/assessment methodologies enable one to see inputs and outputs each step of the journey from raw material extraction through each processing step



System boundaries in life cycle assessment. Ideally, all processes are included in a so-called cradle-to-grave boundary. The system boundary can further be divided into foreground and background systems. The foreground system is here defined as the part that is "under control," i.e., within the design space.

Kleinekorte, J & al. *Annu. Rev, Chem. Biomol. Eng.* **2020**, *11*, 20.1-20.31

LCA/LCI

Different environmental impact categories:

An impact category makes it possible to come to a single metric for climate change

Impact category / Indicator	Unit	Description
Climate change – total, fossil, biogenic and land use	**kg CO_2-eq**	Indicator of potential global warming due to emissions of greenhouse gases to the air. Divided into 3 subcategories based on the emission source: (1) fossil resources, (2) bio-based resources and (3) land use change.
Ozone depletion	kg CFC-11-eq	Indicator of emissions to air that causes the destruction of the stratospheric ozone layer
Acidification	kg mol H+	Indicator of the potential acidification of soils and water due to the release of gases such as nitrogen oxides and sulphur oxides

Eutrophication – freshwater, Eutrophication – marine, Eutrophication – terrestrial, Photochemical ozone formation, Depletion of abiotic resources – minerals and metals, Depletion of abiotic resources – fossil fuels, Human toxicity – cancer, non-cancer, Eco-toxicity (freshwater), Water use, Land use, Ionizing radiation, human health, Particulate matter emissions

LCA/LCI

The case of Climate change category:

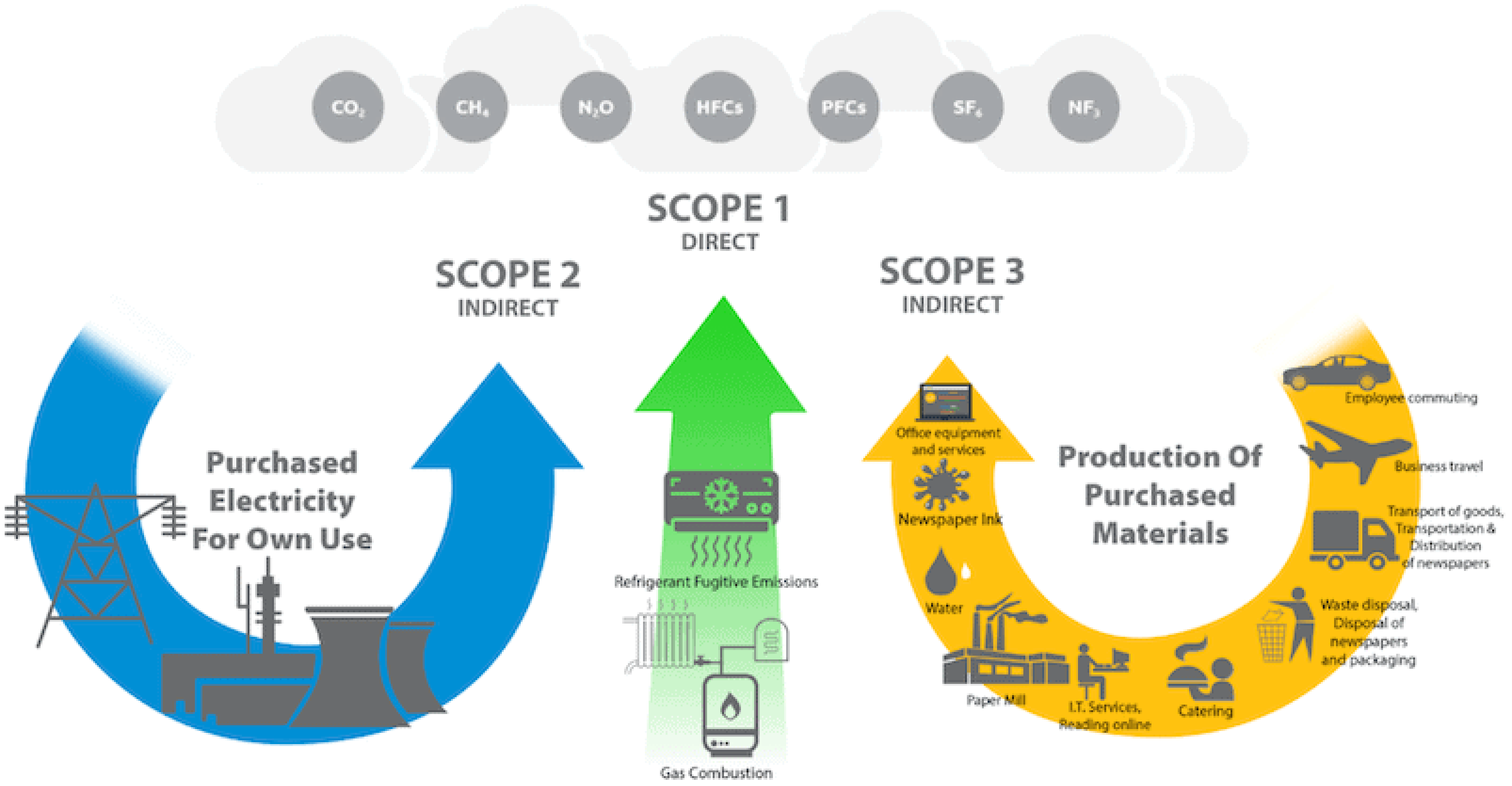
Different emissions that cause the same impact are converted into one unit that translates into one impact category.
For example: CO_2, CH_4, N_2O, HFC, PCF, etc.

An impact category makes it possible to come to a single metric for climate change

Greenhouse gas (GHG)	Equivalent in kg CO_2-eq of the release of 1 kg of the GHG
CO_2 from fossil source	1
CO_2 from renewable carbon	0
CH_4	28
N_2O	273
PF_6	25’200
HFC-23	14’600

LCA Analysis

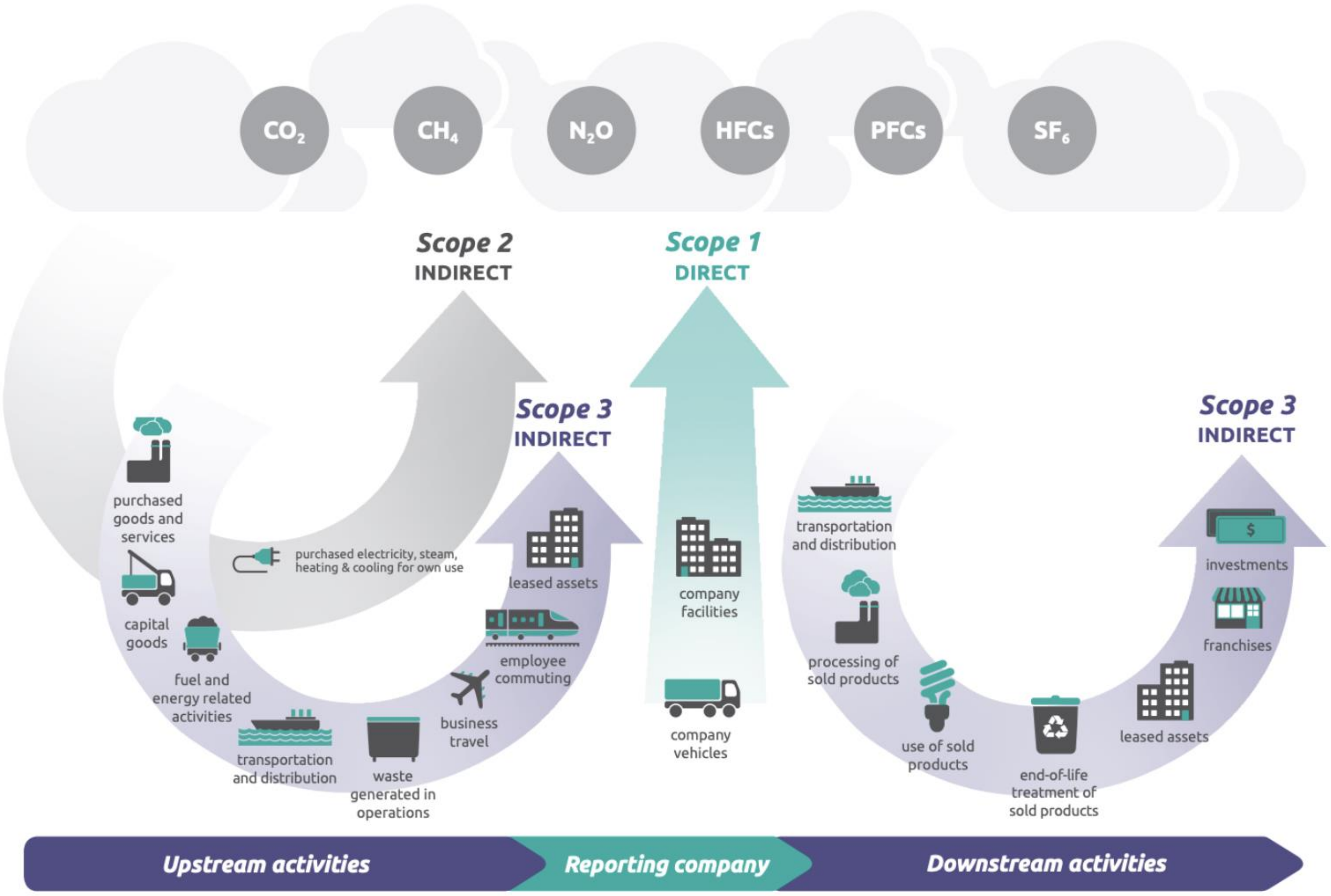
Carbon emission Impact



Standart: ISO 14040:2006.

LCA Analysis

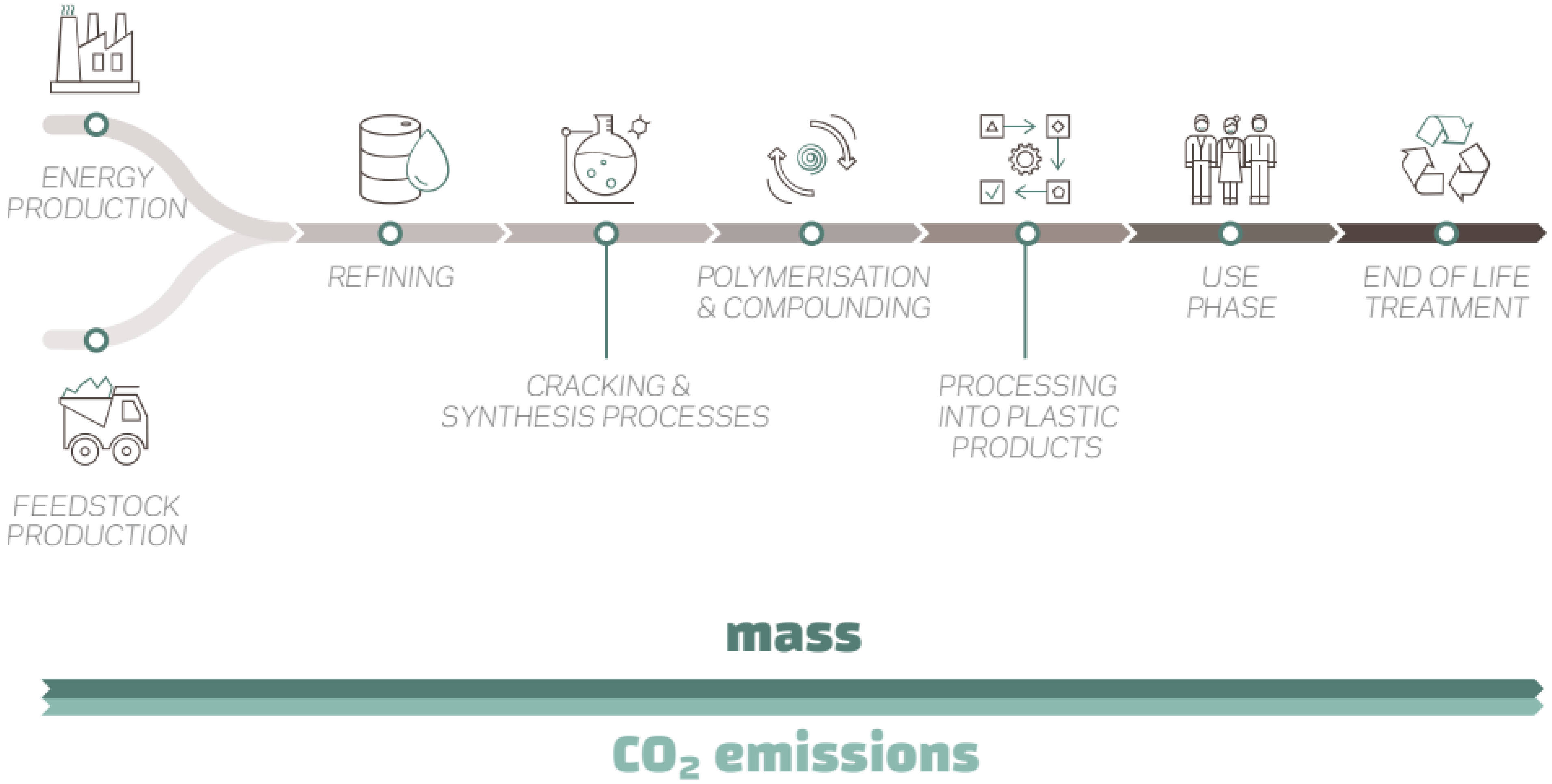
Carbon emission Impact



Collett, K. A., Fry, E., Griggs, S., Hepburn, C., Rosetto, G., Schroeder,
N., Sen, A., and Williams, C. (**2023**). Cleaning up Cleaning: policy and stakeholder interventions to put household formulations on a pathway to net zero. Oxford Smith School; Working Paper 23-07
http://www.smithschool.ox.ac.uk/

Circular Economy-Recycling

Material Flow Analysis



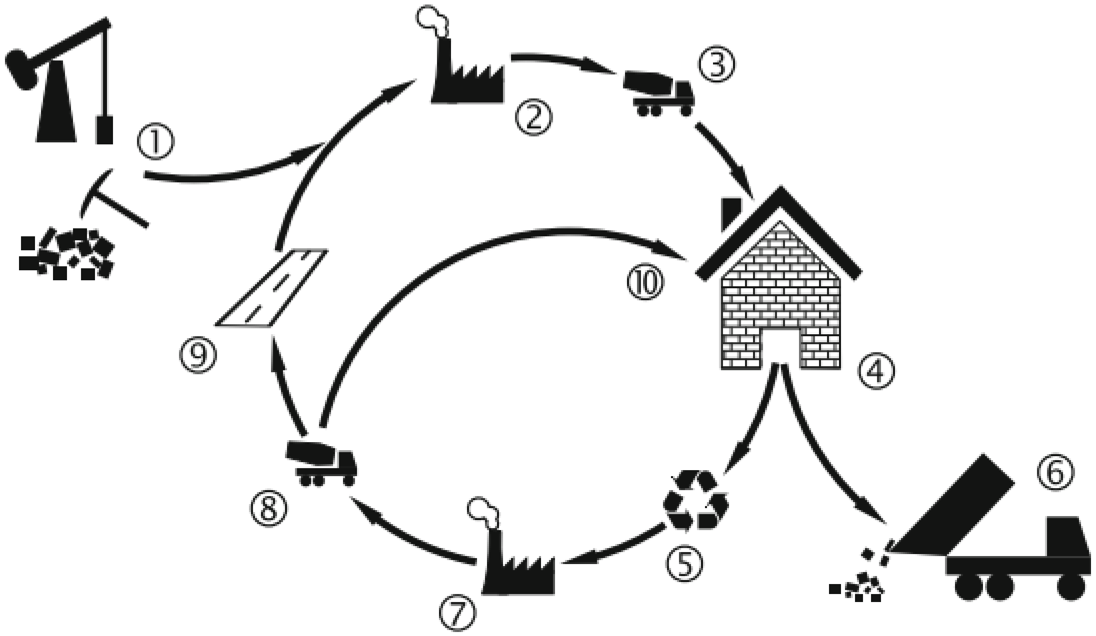
https://cefic.org/

Green Metrics: Real-Life Tools

Sustainable Chemistry
LCA: Life Cycle Assessment.

Life cycle of non-renewable materials:

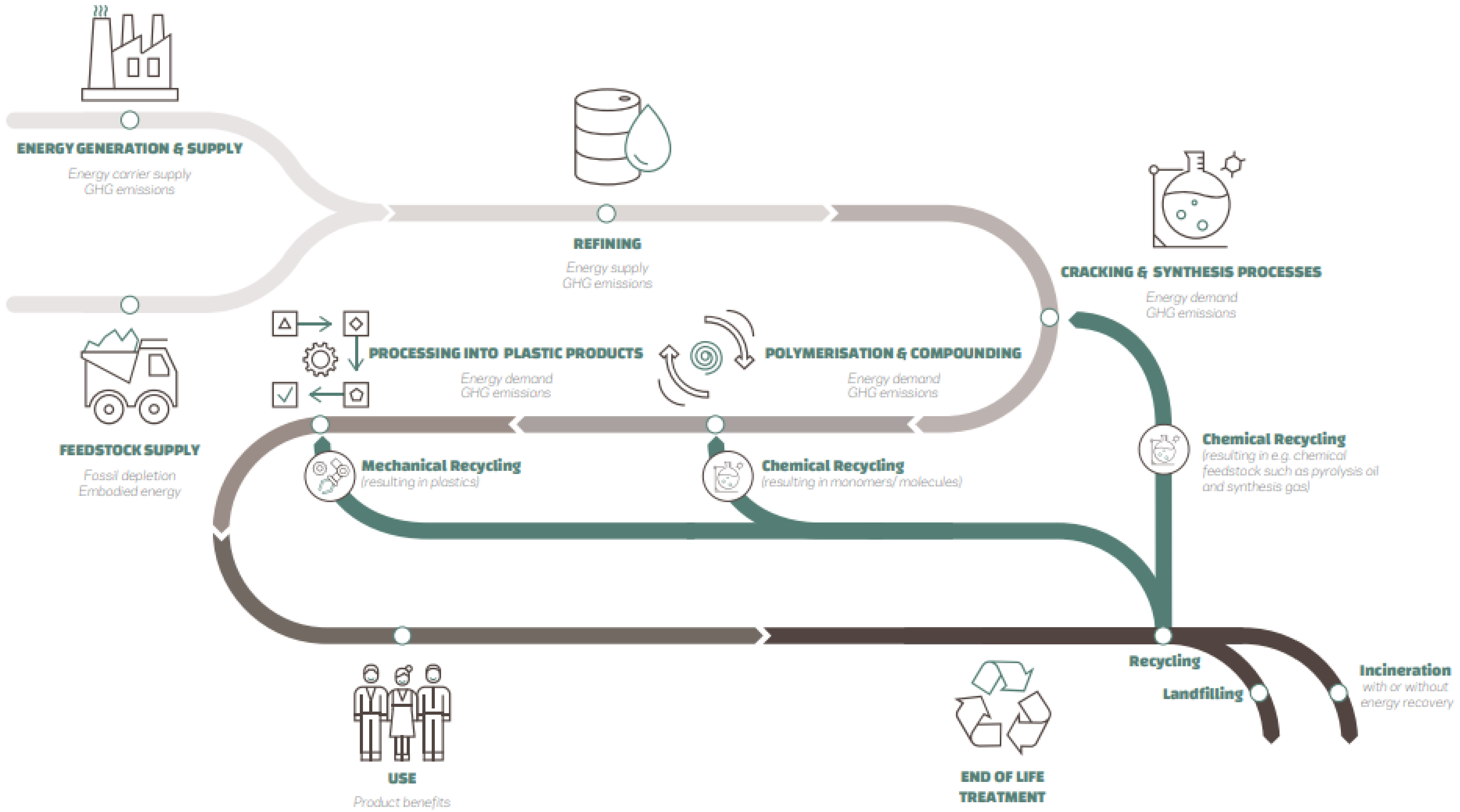
1. Extraction of raw material
2. Manufacturing
3. Processing
4. Use phase
5. Recycling
6. Landfilling/waste production
7. Secondary manufacturing
8. Secondary processing for reuse
9. Second use phase
10. Second reuse phase



[Open Access: Biomaterials for Building Skins | SpringerLink]

Circular Economy-Recycling

Value chain in polymers: Mechanical & Chemical recycling



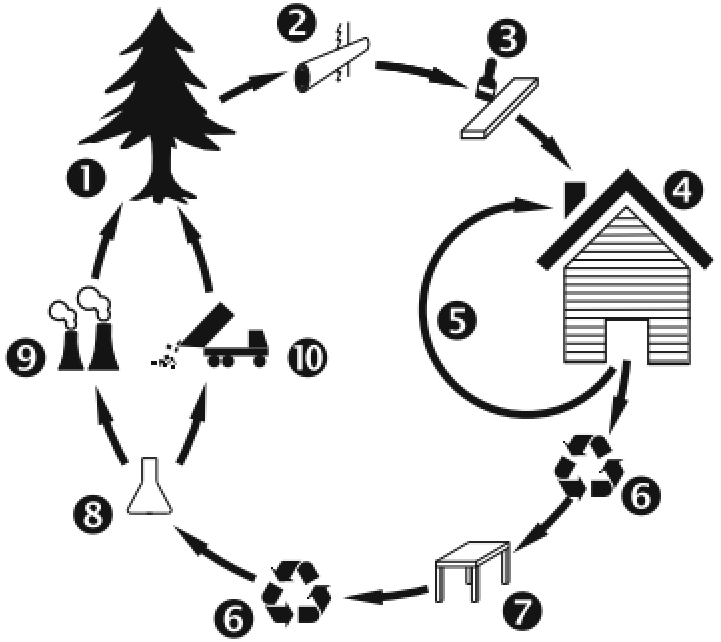
https://cefic.org/

Green Metrics: Real-Life Tools

Sustainable Chemistry
LCA: Life Cycle Assessment.

Life cycle of renewable materials:

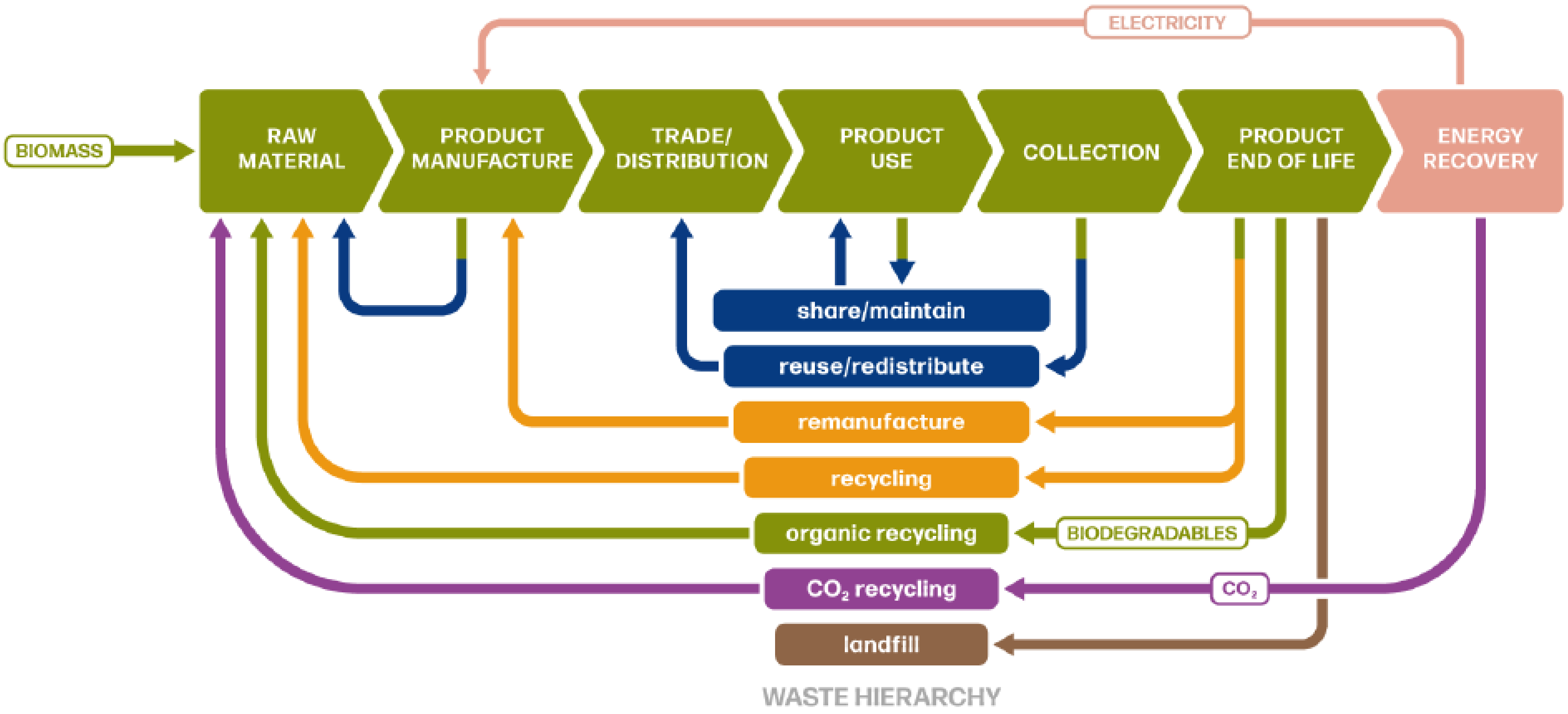
1. Harvesting
2. Primary processing
3. Secondary processing
4. Use phase
5. Reuse
6. Recycling
7. Second use phase
8. Cascading to tertiary use
9. Energy generation
10. Landfilling, closing the biological and technical metabolism



[Open Access: Biomaterials for Building Skins | SpringerLink]

Circular Bioeconomy

Value chain in polymers: Mechanical & Chemical recycling



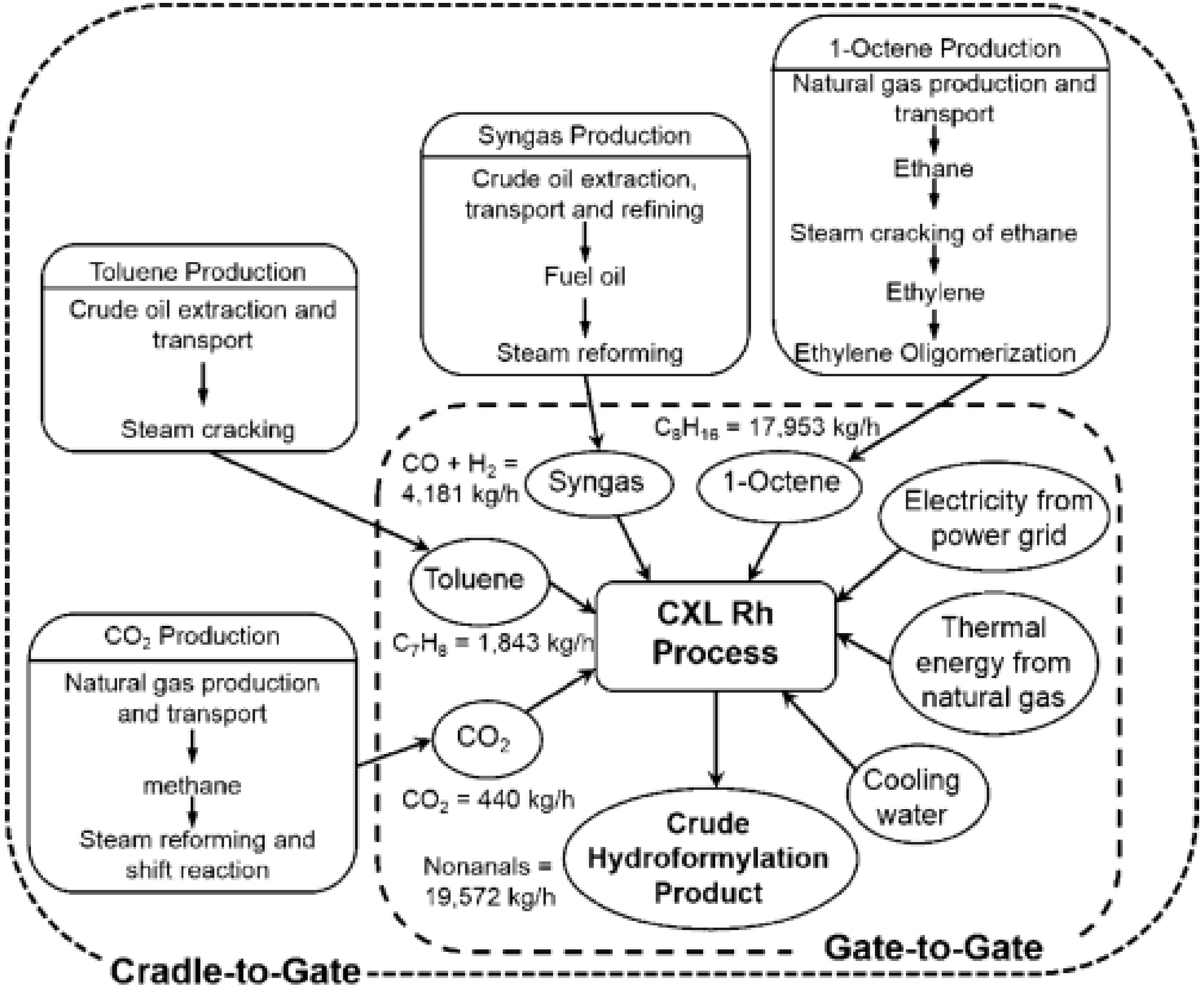
https://renewable-carbon.eu/graphics

Circular economy action plan - European Commission (europa.eu)

LCA Analysis

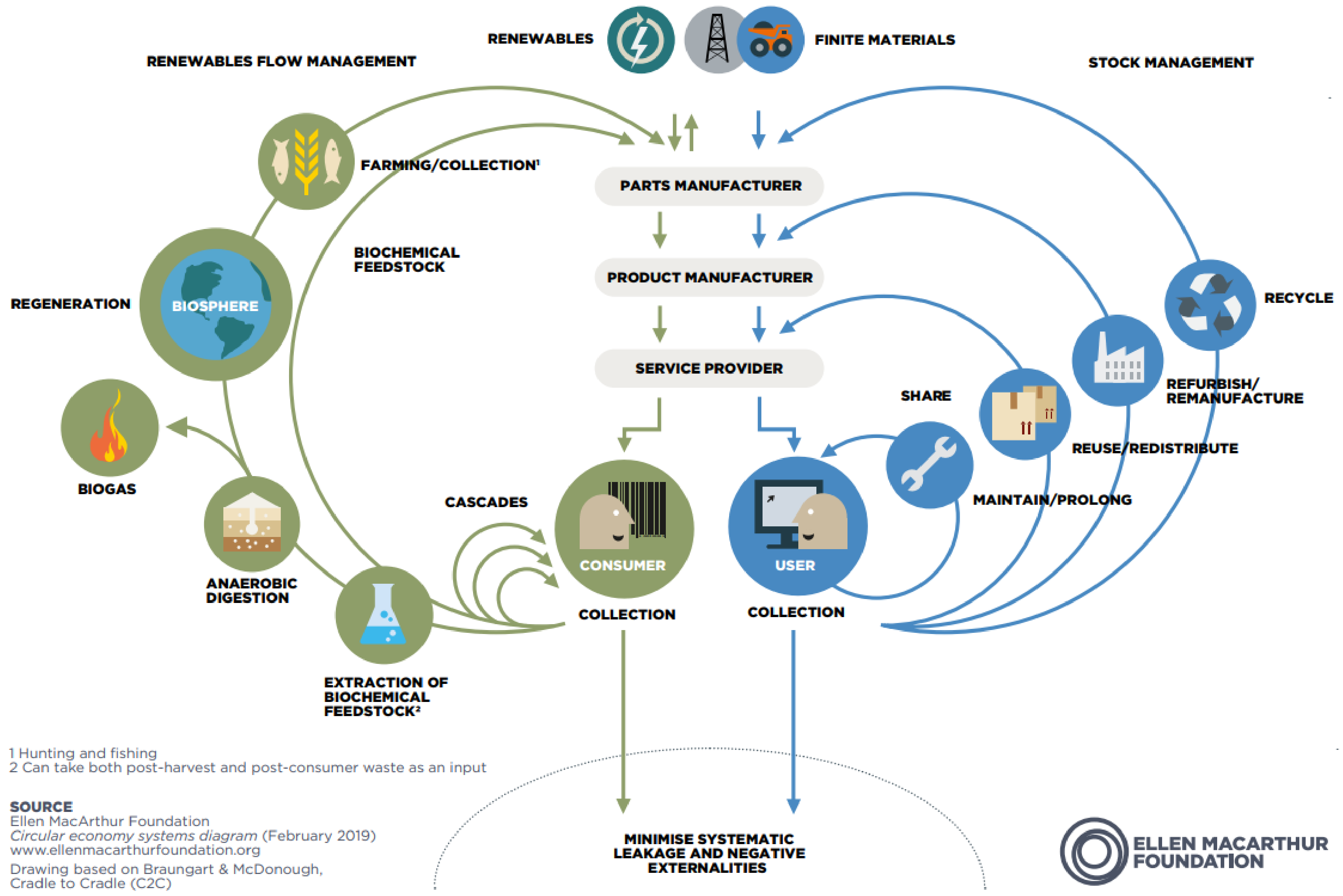
Analysis

Hydroformylation of Olefin



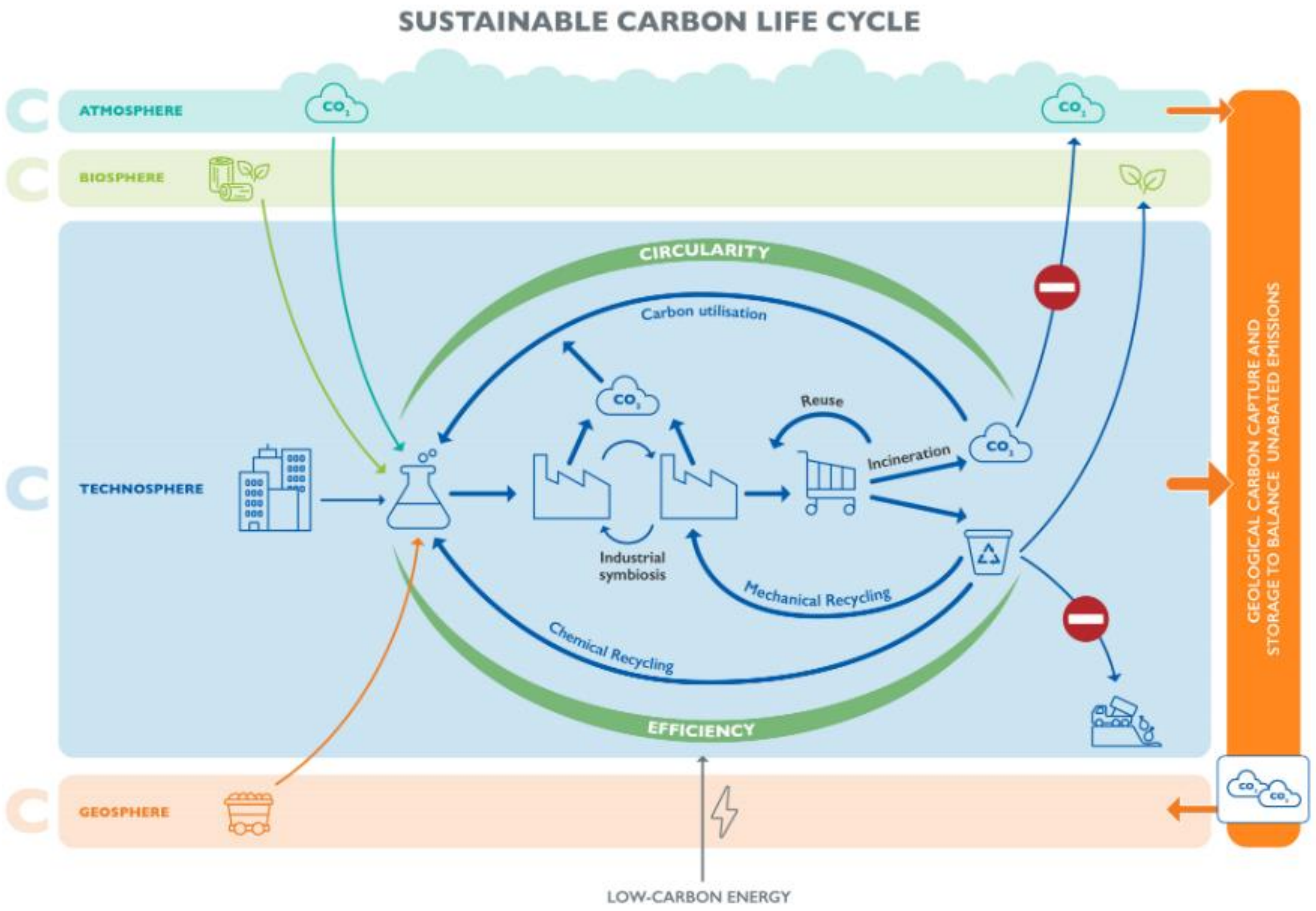
Xie, Z. *et al. ACS Sustainable Chem. Eng*. **2014**, *2*, 2748.

Circular Bioeconomy



[The Butterfly Diagram: Visualising the Circular Economy (ellenmacarthurfoundation.org)](https://ellenmacarthurfoundation.org)
https://renewable-carbon.eu/graphics

Sustainable Carbon Cycles



Critical Review:
Dees, J. P. *et al. Green Chem.*, **2023**, *25*, 2930.

https://cefic.org/

Green Metrics & Sustainability

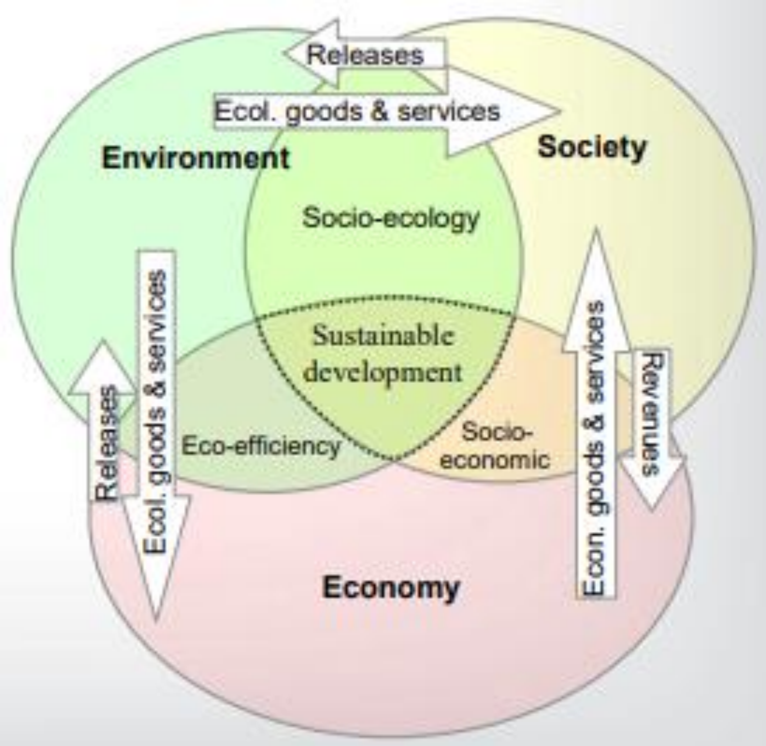
Global overview:

Green metrics:
Tools to compare different processes but no absolute values
Not possible to conclude that a process is green !

Still a lot of work to be done: harmonize all the metrics, rules to use them
What about Societal Impact, Justice, Intergenerational Justice, Boundaries, etc

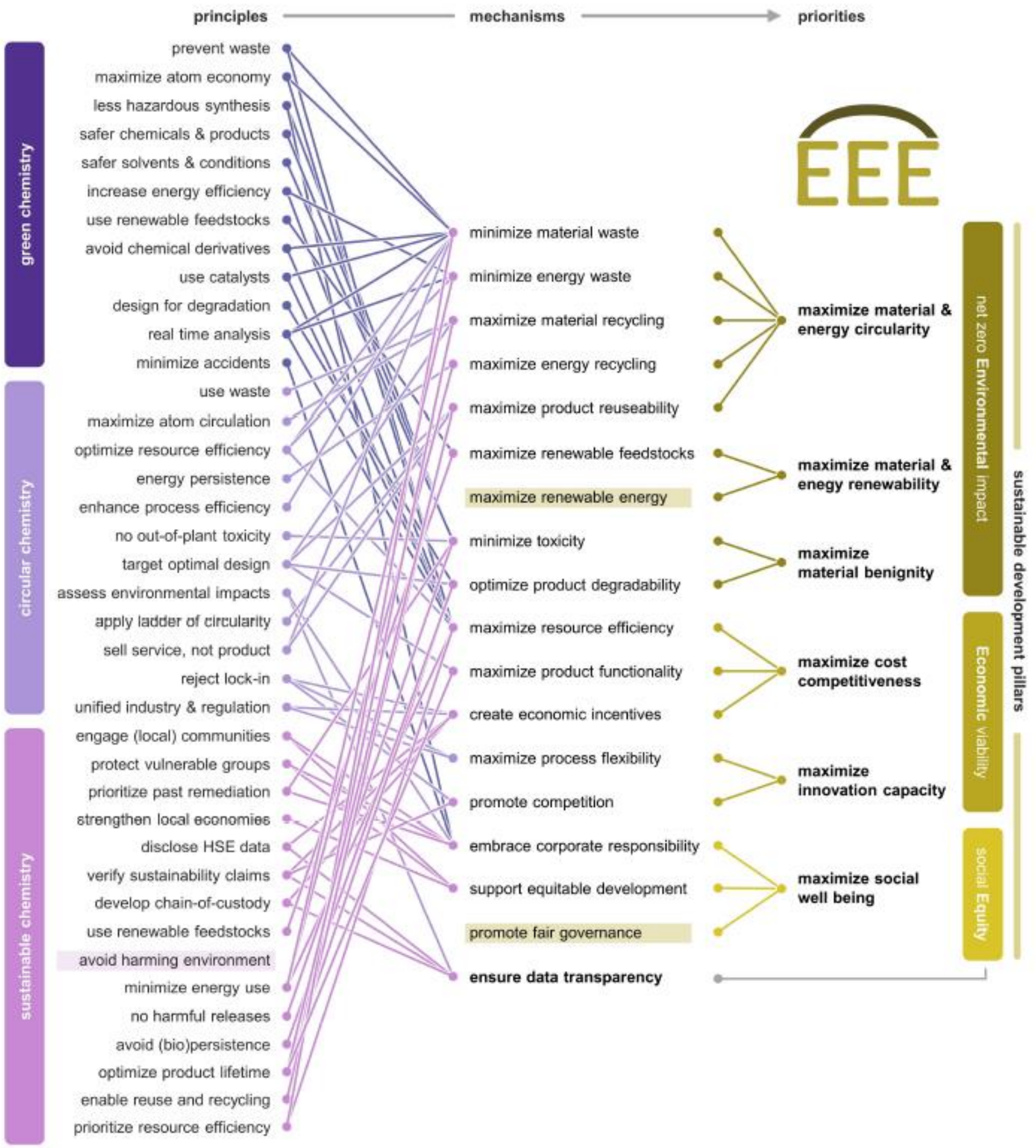
What are the values to prioritize to include/exclude?

After CO_2: Water, landfill, toxicology (endocrine disruptor…)



https://cfpub.epa.gov/si/si_public_file_download.cfm?p_download_id=542328&Lab=CESER
(accessed August 23, 2023).
Sheldon, R. A. *ACS Sustainable Chem. Eng.* **2018**, *6*, 32–48.
Diverse values of nature for sustainability, Nature **2023**, *620*, 813.
Kunming-Montreal Global Diversity Network: https://www.cbd.int/gbf/

Green Metrics & Sustainability



S. Mitchell, A. J. Martín, G. Guillén-Gosálbez, J. Pérez-Ramírez *Angew. Chem. Int. Ed.* **2024**, *63*, e202318676.

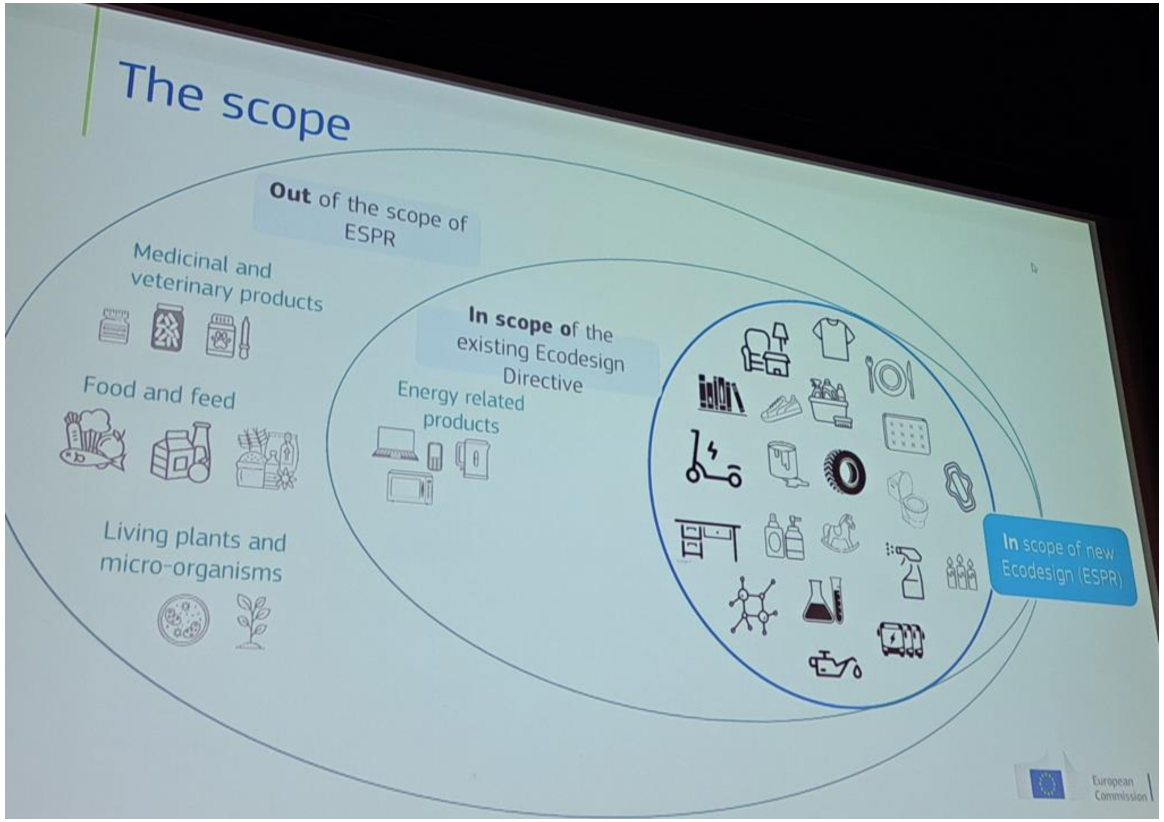
Green Metrics & Sustainability: Future ?

For example: Europe

NEW Ecodesign framework: ESPR (replace the Eccodesign) in force 2025 based on 2024 numbers.

And **CBAM**: **C**ross **B**order **A**djustment **M**echanism
cement, iron & steel, aluminum, fertilizers
(ammonia, urea, nitric acid, ammonium nitrate)
and electricity.

January 2030: Evaluation if chemicals and polymers.



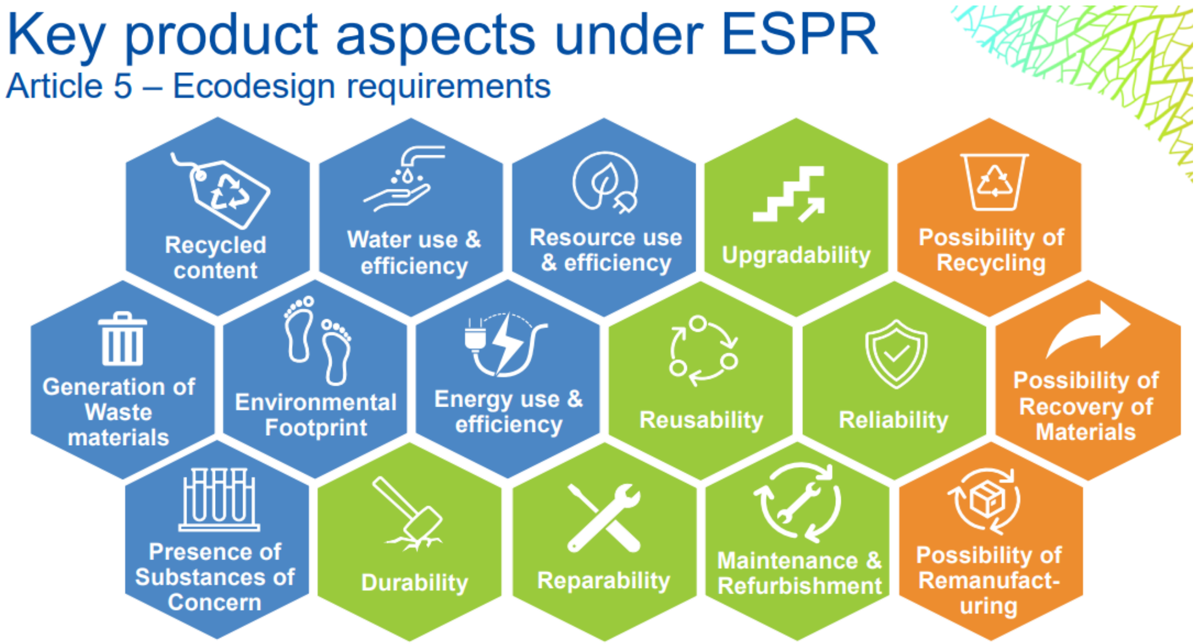
https://commission.europa.eu/energy-climate-change-environment/standards-tools-and-labels/products-labelling-rules-and-requirements/sustainable-products/ecodesign-sustainable-products-regulation_en
https://www.reachlaw.fi/the-ecodesign-for-sustainable-products-regulation-espr/

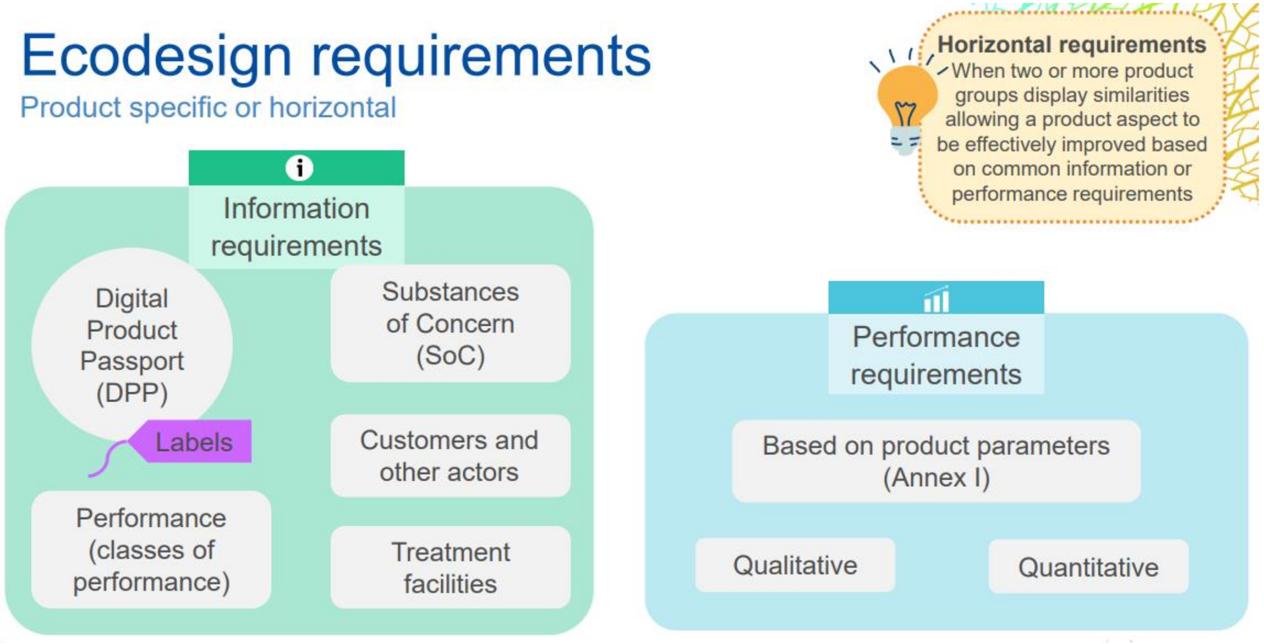
Green Metrics & Sustainability: Future ?

For example: Europe/NEW Ecodesign framework:

[Link to EU presentation-slides deck]

[Cosmetics - European Commission (europa.eu)]





Green Metrics & Sustainability: Future ?

Using prospective LCA models: IAM-LCA coupling flow [**I**ntegrated **A**ssessment **M**odels]
Future scenarios such as the socioeconomic pathways are used as inputs together with e.g. ecoinvent

Step 1: Ecoinvent data are connected to Integrated Assessment models (IAMs) by creation of a superstructure database.

Step 2: connection between ecoinvent and additional inventories, that represent emerging and future technologies.

Step 3: Export of the database into a common LCA software (Simapro, Brightway2)

Step 4 and 5: Producing LCA resource and environmental indicators (and feeding back into IAM).

Arvesen, A.; Luderer, G.; Pehl, M.; Bodirsky, B. L.; Hertwich, E. G. *Environmental Modelling & Software* **2018**, *99,* 111.
R. Sacchi, T. Terlouw, K. Siala, A. Dirnaichner, C. Bauer, B. Cox, C. Mutel, V. Daioglou, G. Luderer, *Renewable and Sustainable Energy Reviews* **2022**, *160*, 112311.

Green Metrics & Sustainability: Future ?

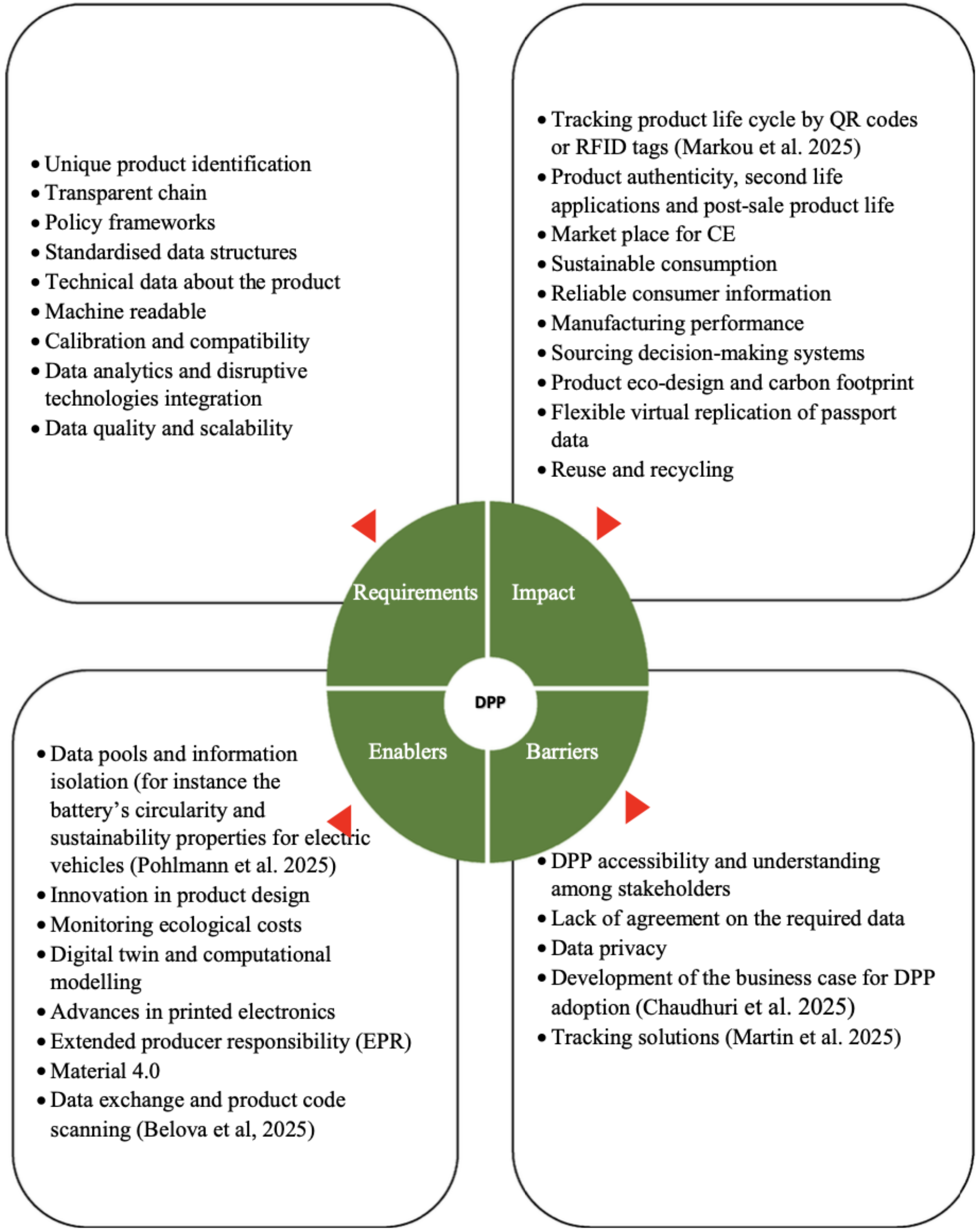
For example: Europe

Digital Product Passport (DPP):

https://commission.europa.eu/energy-climate-change-environment/standards-tools-and-labels/products-labelling-rules-and-requirements/sustainable-products/ecodesign-sustainable-products-regulation_en
https://commission.europa.eu/energy-climate-change-environment/standards-tools-and-labels/products-labelling-rules-and-requirements/sustainable-products/about-sustainable-products_en

Green Metrics & Sustainability: Future ?

Not only Europe
Digital Product Passport (DPP):



Circular Economy and Sustainability, 2025:
Towards an International Digital Product Passport: The New Paradigm of a Worldwide Circular Economy
https://doi.org/10.1007/s43615-025-00690-5

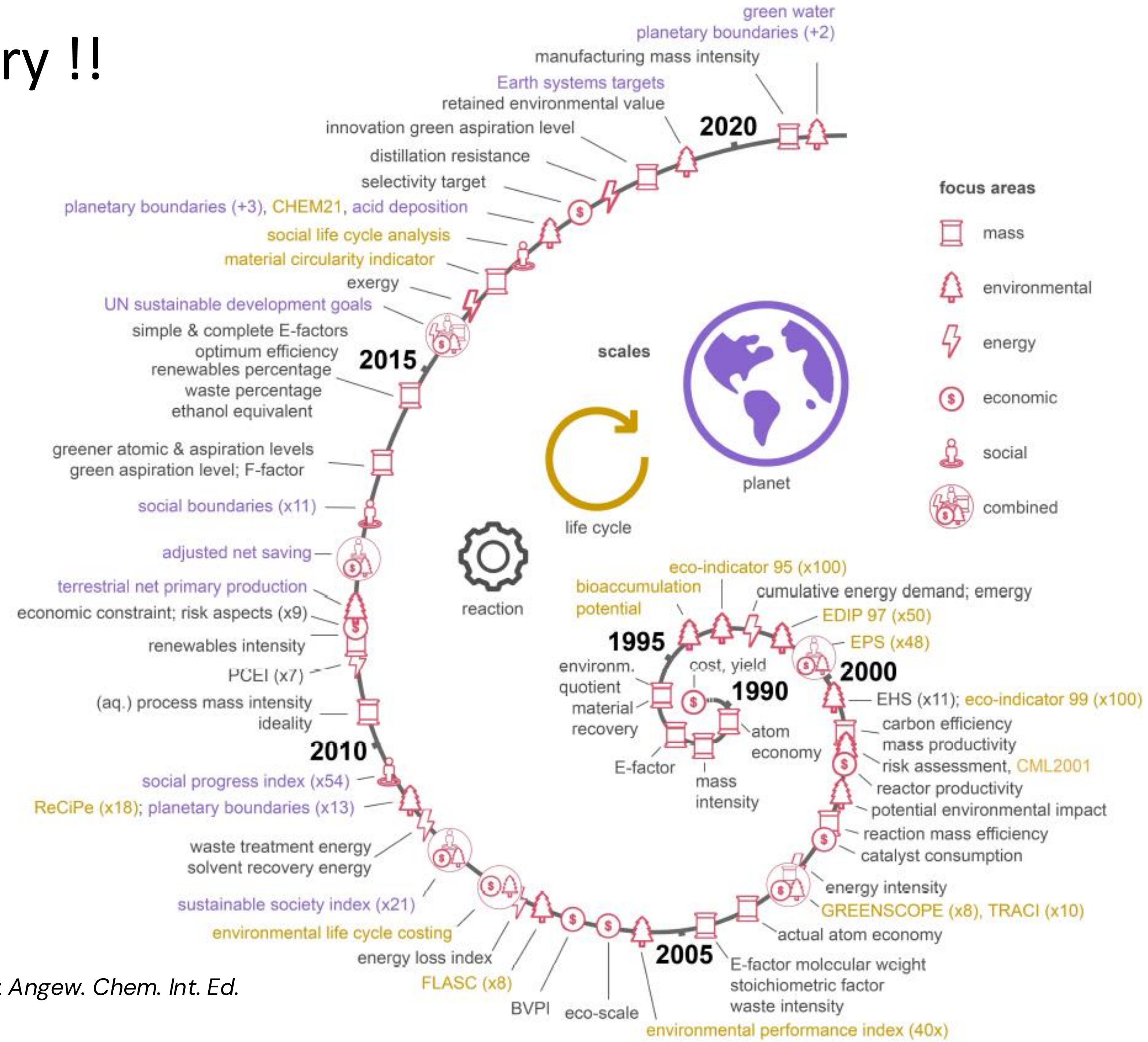
Green Metrics & Sustainability: Future ?

For example: Europe

Digital Product Passport (DPP):

- The new “Digital Product Passport” will provide information about products’ environmental sustainability.
- This information will be easily accessible by scanning a data carrier.
- It will include attributes such as the durability and reparability,
  the recycled content
  the availability of spare parts of a product.
- It should help consumers and businesses make informed choices when purchasing products,
  facilitate repairs and recycling and
  improve transparency about products’ life cycle impacts on the environment.
- The product passport should also help public authorities to better perform checks and controls.

The Never Endind Story !!



S. Mitchell, A. J. Martín, G. Guillén-Gosálbez, J. Pérez-Ramírez *Angew. Chem. Int. Ed.* **2024**, *63*, e202318676.