DPS Better Engineered Solutions

ISPE Ireland Affiliate

Improving the Sustainability of Cell-based Vaccine Production

ISPE Ireland Student Chapter, Webinar, 14th April 2021

Bill Whitford

DPS Group - Life Science Strategic Solutions Leader

DPS Group

- A leading global Architectural, Engineering and Consulting Company
- Advanced therapeutics focus
- 2000 People in 16 offices worldwide

Agenda

Single-use cell-based vaccine production challenge

Life cycle assessment: identify / quantify impacts

Insights to guide responsible post-use handling choice

Single-use vaccine production challenge

Vaccines employing cultured cells I

J&J's vaccine

- PER.C6 cell line technology
- Janssen's AdVac viral vector technology
  A high yielding vaccine mfg. platform
- "Scalable and fully industrialized"

Janssen COVID-19 Vaccine
(Ad26.COV2.S)

AdVac® and PER.C6® Technology of the Janssen COVID-19 Vaccine

https://www.janssenmd.com/printpdf/janssen-covid19-vaccine/pharmacology/mechanism-of-action/advac-and-perc6-technology-of-the-janssen-covid19-vaccine?pdf-version=

BioProcess International

UPSTREAM PROCESSING DOWNSTREAM PROCESSING MANUFACTURING

COVID vaccines: Why J&J could have market advantage over others

by Dan Stanton
Thursday, January 28, 2021 8:03 am

Tried and tested technologies, a single-dose regimen, and a simple cold-chain infrastructure place Johnson & Johnson's potential COVID-19 vaccine at an advantage over the current approved offerings.

Johnson & Johnson (J&J) has said it plans to present results of its COVID-19 candidate JNJ-78436735, also known as Ad26.COV2-S, recombinant, in the next few days.

"Being in the final stages of a robust 45,000-person study, analytics will be completed, and we plan to report out the results by early next week," CFO Joe Walk said on an investor call Tuesday.

https://bioprocessintl.com/bioprocess-insider/global-markets/covid-vaccines-why-jj-could-have- market-advantage-over-others/

Vaccines employing cultured cells II

Vaccine Type	Description
Attenuated whole cell	Genetically weakened pathogenic bacteria
Recombinant bacterial vectored	Attenuated or inactivated bacteria present heterologous antigens
Live attenuated virus	Genetically weakened pathogenic virus
Recombinant viral vectored	Attenuated or inactivated virus present heterologous antigens
Killed (inactivated) cells or virus	Pathogenic bacteria or virus physically or chemically disabled
Subunit	Containing free (or vectored) pathogen antigens (e.g. capsid protein, polysaccharides, or toxins)
Recombinant subunit	Heterologous antigens expressed in prokaryotic (e.g., E. coli) or eukaryotic (e.g., animal) cells
Polyvalent	Immunizing against more than one serotype-specific epitopes
Polysaccharide	Free polysaccharides that elicit B-cell immune responses
Conjugate	Weak antigen (e.g., polysaccharide) covalently attached to a stronger antigen (e.g. a protein)
Heterotypic (Heterologous)	One pathogen is introduced in order to provide protection against a different one
Synthetic	Chemically synthesized Protein / glucan / nucleic acid antigens and cell-based vectoring
Hapten Conjugate	Small molecules that elicit a specific immune response when attached to large carrier molecules
Dendritic cell	In vivo or in vitro stimulated DCs or precursors induce antigen specific T cell response
DNA	DNA coding for an antigen's gene from a pathogen inserted into the vaccine recipient's cells
RNA	mRNA coding for an antigen's gene from a pathogen inserted into the vaccine recipient's cells
Viral vectored	Live viruses carry nucleic acid coding for antigens that are expressed in the recipient's cells
Chimeric	Typically, substituting pathogenic genes from the target pathogen to a related, but safe organism

Vaccines employing cultured cells II

Vaccine Type	Description
Non-env. virus-like particle	Antigenic proteins that self-assemble into empty virus capsids
Enveloped virus-like particle	Self-assembling antigenic proteins establishing an envelope by budding from an animal cell
Subviral particles	A subunit vaccine as a VLP, but with truncated capsid proteins
Combination VLP	Subunit VLP presenting multiple recombinant or covalently coupled antigens or epitopes
Exosome/EV based delivery	Exosomes/EVs harboring antigenic protein, glycans or a nucleic acid from pathogen
Exosome/EV display	Targeting antigens to surface of extracellular vesicles or exosomes
Synthetic nanoparticle	Antigen functionalized 1-200 nM lipid, protein, carbon, mineral, metal or nanopolymersomes
Synthetic microparticle	Antigen functionalized 1-1000 μm lipid, protein, carbon, mineral, metal or polymer particles
Liposome	Spherical phospholipid bilayers enclosing an aqueous core and presenting or harboring antigen
Emulsion	Stable dispersions of hydrophobic fluids including antigens in buffer
Toxoid vaccines	Vaccine against inactivated (detoxified) toxic compounds rather than the pathogen itself
Protein complexed	Conjugate vaccines using stimulatory protein complexes (as from microbes) as a carrier
Dendritic cell	Stimulating DCs in vivo or ex vivo against the target and then infusing them into the recipient
T-cell receptor (TCR) peptide	Peptides derived from amino acids of TCRs that down-regulate expression of those TCRs
Prime-boost	Inoculating w/ one type of vaccine, then strengthening response with another type
Dermal	Mechanically induced migration of vaccine through the skin
Transcutaneous	Topical application of vaccine to intact skin that chemically migrates internally
Non-env. virus-like particle	Antigenic proteins that self-assemble into empty virus capsids

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Bioprocessing transitions to SU technologies

Stainless-steel facilities

Image courtesy of Sartorius

Ecosystem quality

Natural resources

Human health

Single-use facilities

Image courtesy of Sartorius

- Continued shift to SU in cell-based vaccine production
- How does SU technology support sustainability expectations?
- What are all the environmental trade-offs associated with the shift?

SU product categories / operational criteria

Consumer Convenience

- Foam food containers
- Plastic grocery bags
- Straws and spoons
- Cans and pouches

Medical / Pharma Needs

- Platform flexibility
- Entity flexibility
- Build time
- CapEx
- OpEx
- Total output
- Sterility assurance
- Mfg. sustainability

Business / Regulatory

- Shortages of filters / bags
- Change control process
- SUS shipping / storage
- Operational geography
- War powers act

Sustainability: a complex / competitive endeavor

Burden trade-offs between distinct concerns

E.g., which is most significant?

- Landfill operation
- Atmospheric carbon

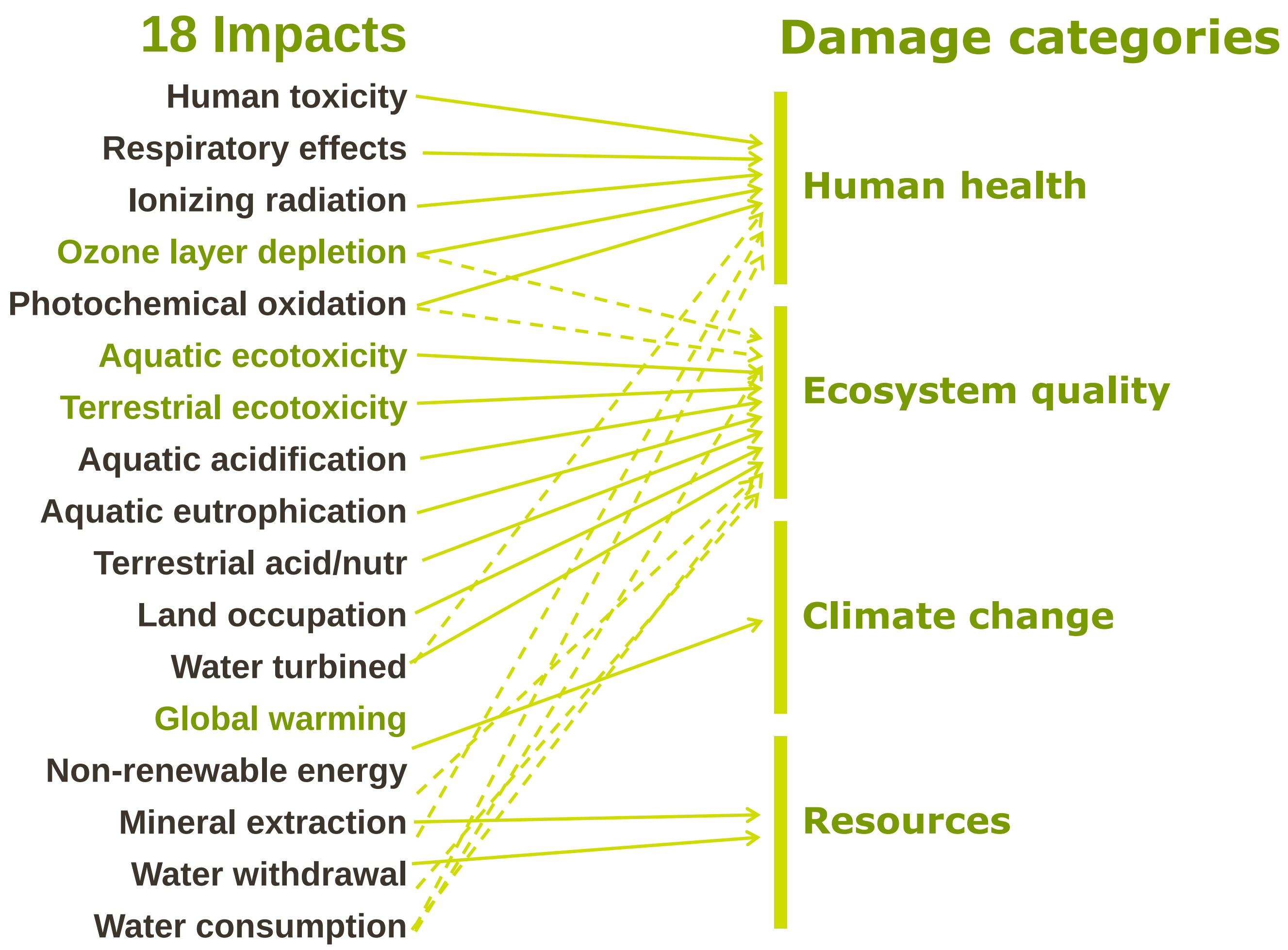
E.g., best option for complex / tainted plastics

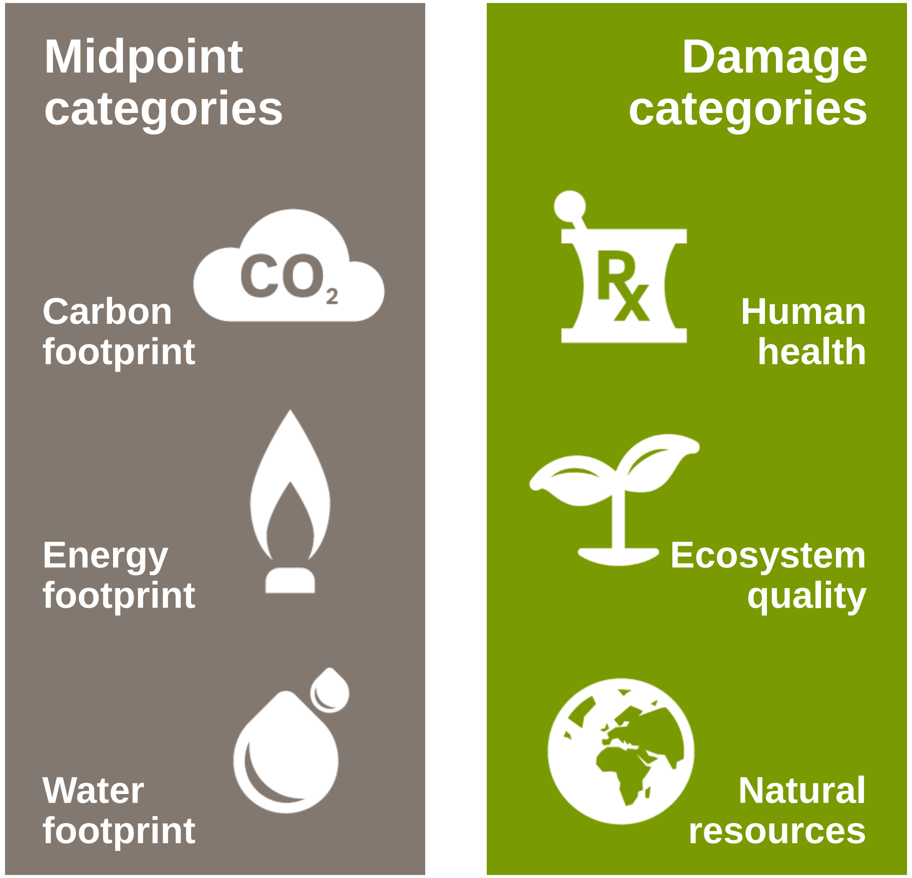
- Re-use in national repurposing center?
  - High process / transport carbon burden
  - Only delays carbon release
- Use for local power generation?
  - Low process / transport carbon burden
  - Releases all carbon now

LCA

A detailed, rigorous approach to environment sustainability

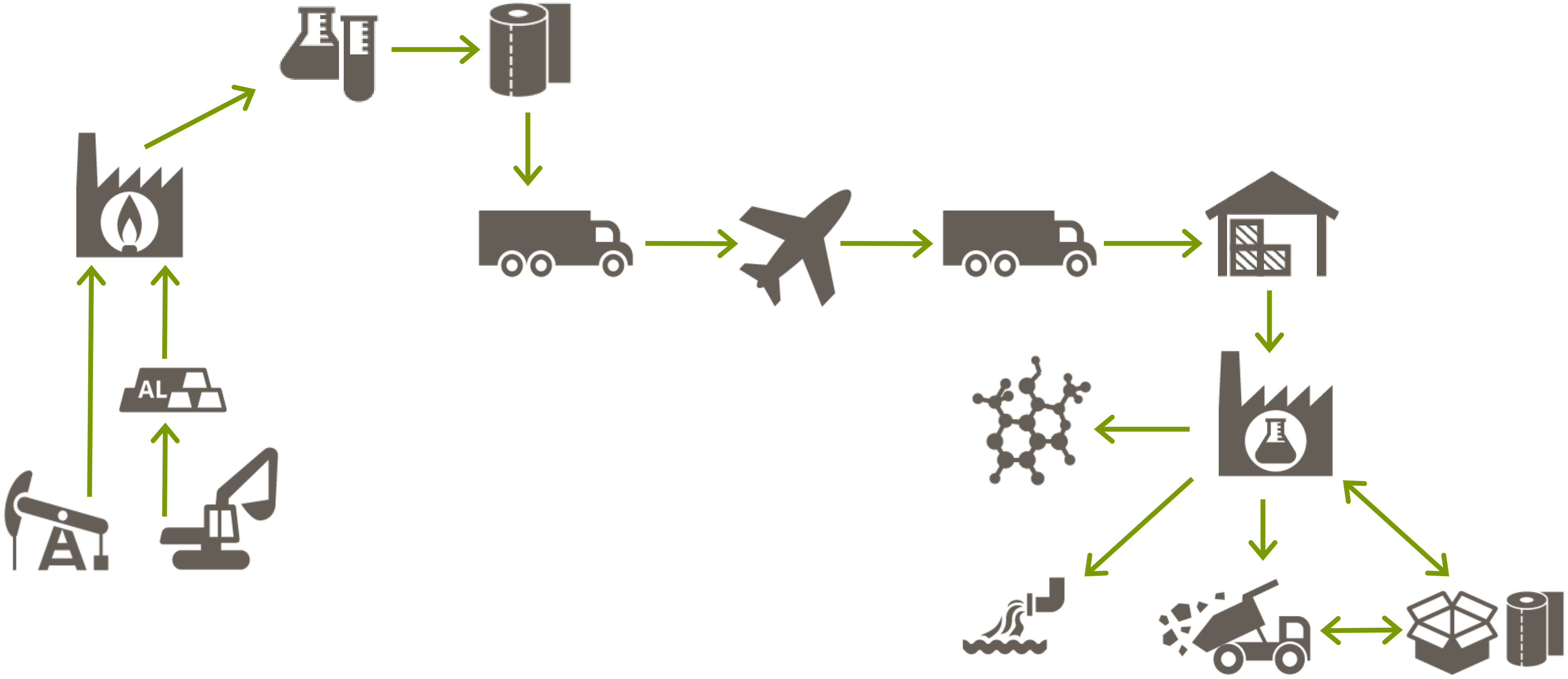
Environmental impact assessment





Jolliet O. *et al*, IMPACT 2002+: a new life cycle impact assessment methodology, *Int. J. Life Cycle Assess* **8(6)**, 324-330 (2003) as adapted by Quantis in version Q2.22 of IMPACT 2002+: User Guide

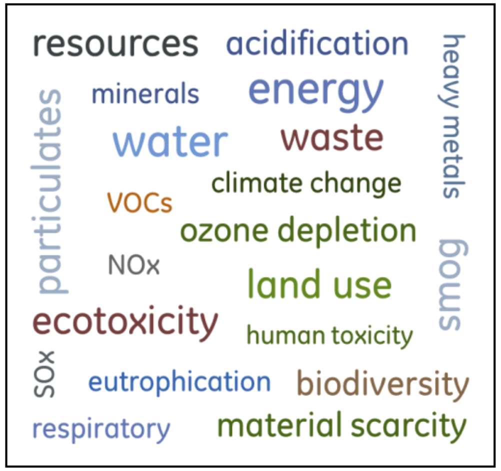
Life Cycle Assessment: mining to destruction

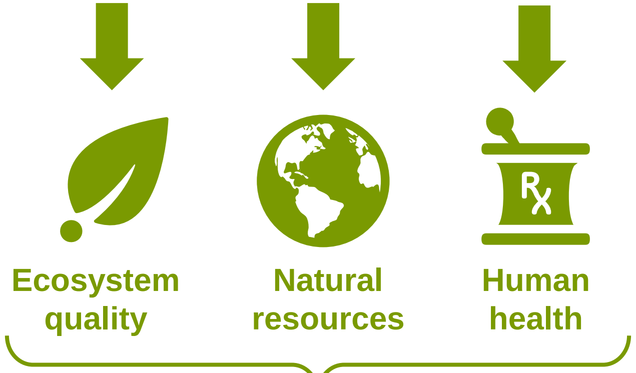


LCA: Impacts through vaccine mfg. life cycle

LCA: Life Cycle Assessment

More than just carbon footprint





Areas of protection (damage categories)

Understanding impact of products / services across value chain

- Support decisions
- Evaluate alternatives
- Prioritize opportunities
- Mitigate environmental issues

LCA study results

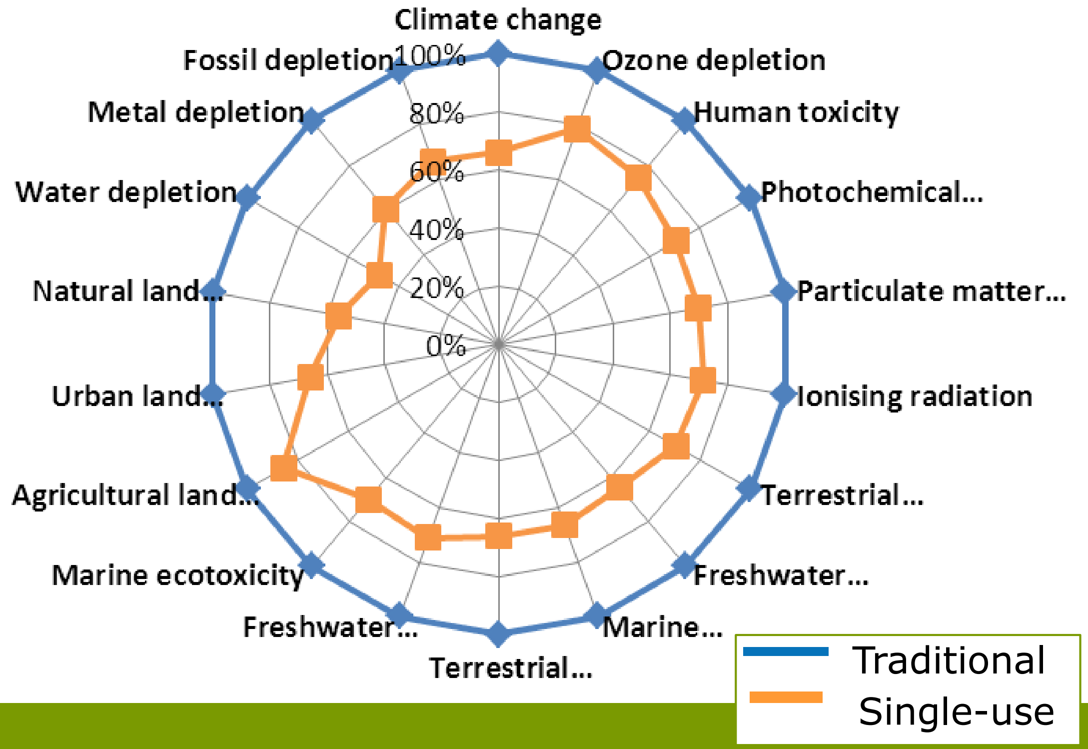
GE 2012 life cycle assessment

Purpose / driver of life cycle assessment (LCA)

- Compare multi-use vs. single-use impacts

Results / lessons learned

- SU exhibits lower impact across full life cycle
  - Reduction of WFI, process water, steam
  - Less energy consumption, water fouling, CIP / SIP
- Various SU post-use impacts negligible compared to use-phase and supply chain activities
- Study was subjected to a third-party critical panel review per ISO 14040-44

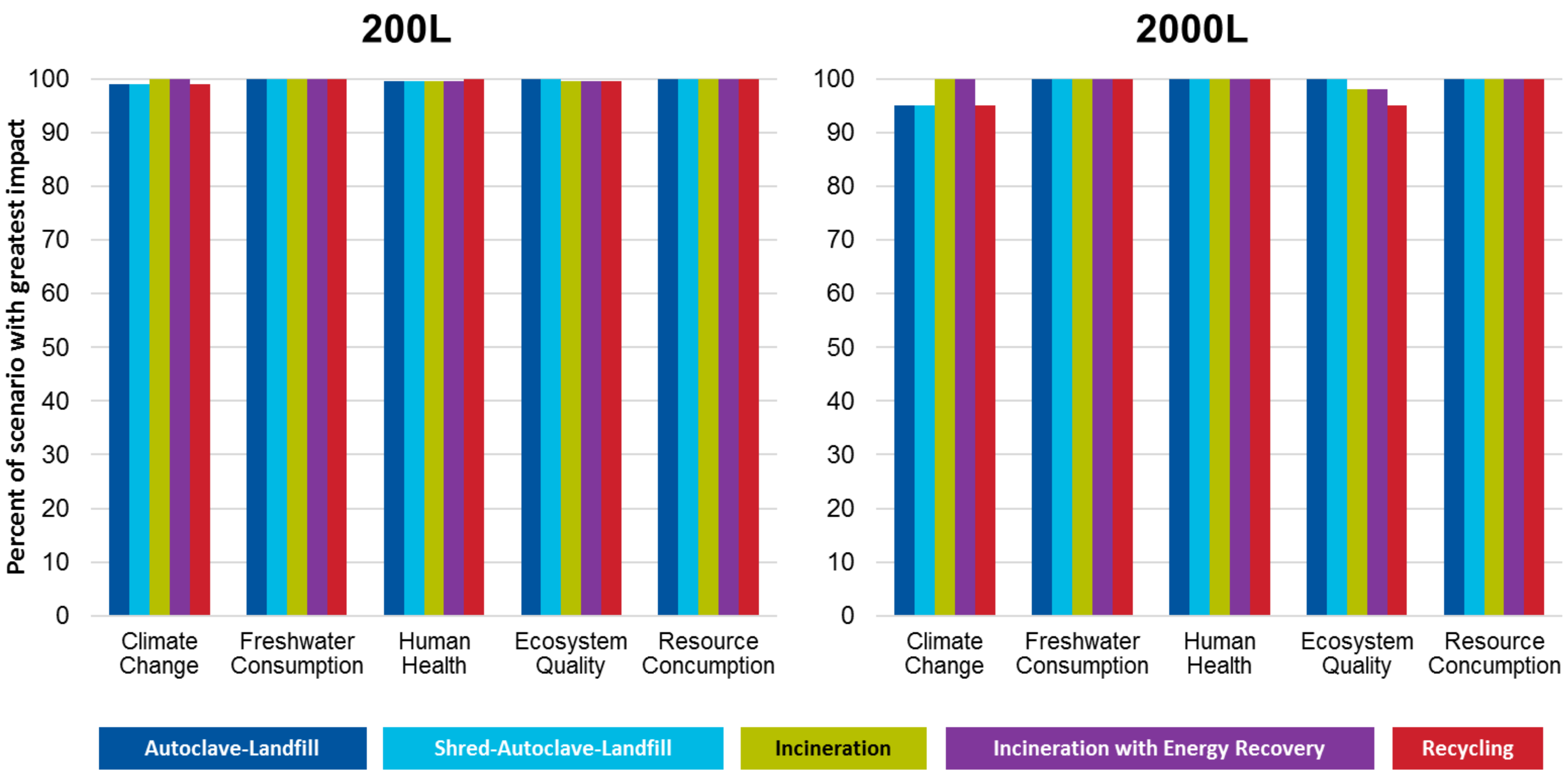


Result was unexpected, counterintuitive and only accessible through detailed LCA

Pietrzykowksi M. *et al*, An Environmental Life Cycle Assessment Comparison of Single-Use and Convention Process Technology for the Production of Monoclonal Antibodies, *J. Clean. Prod.* 41, 150-162 (2013).

Comparative impact: alternative disposals

Process	mAb
	Traditional
	Single-use
	Hybrid
Location	Boston
	LA
	Sao Paolo
	Istanbul
	Cork
	Dortmund
	Shanghai
Scale	200 L
	500 L
	2000 L
	2 x 2000 L



An Environmental Life Cycle Assessment Comparison of Single-Use and Conventional Bioprocessing Technology. GE Healthcare Life Sciences: Uppsala, Sweden, 2013; http://bioprocess.gelifesciences.com/~/media/bioprocess/documents/

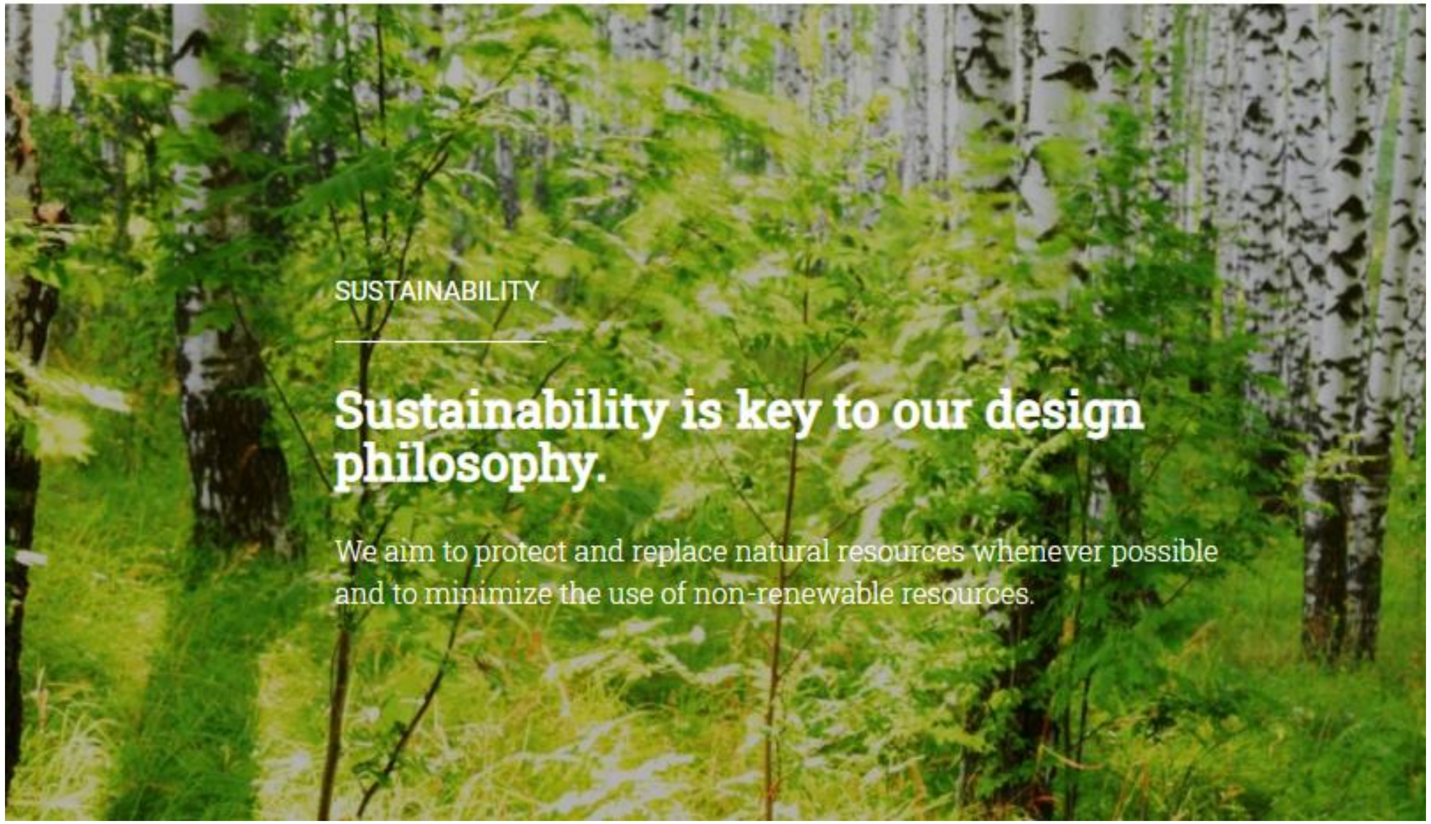
LCA study conclusions

Generalizations: comparing classical to SU

- SU has lower environmental impact over comprehensive life cycle
- Greatest impact observed during the use-stage for both technologies
- Water usage (and consequences) was lower for SU in all life-cycle stages
- End-of-life disposal environmental impacts were higher in the SU systems
- Post-use impacts were negligible, in an overall context of the entire life cycle
- CIP / SIP and WFI energy demands are greatest burdens in classical systems
- Distance / mode of transport from manufacturer drives greatest burden from SU
- Supply-stage carbon/energy impact higher for SU, due to manufacture/transport
- No significant differences were observed between entity types, production scale or mixed modes
- Facility geographic location is largest environmental impact factor due to transport and power grids

SU materials post-use considerations

Materials post-use handling considerations



Parameters considered

- Type of plastics employed
- Used materials at location
- Environment burden type
- Cost of standard disposal
- Best choice available now
- Cost of green alternatives
- GMOs DNA contamination
- Traces of active ingredient
- Distance to recycling plant
- National and regional laws
- Corporate goals/obligation
- Customer/societal demand

Improving the SU vaccine mfg. footprint

Efficient application

- Reduce SU pieces
- Employ smart packaging
- Reduce secondary packaging
- Re-engineer process using less
- Longer shelf life of consumables
- Re-engineer materials reducing mass
- Environmental footprint-based design
- Exploit process intensification serendipity
- Employ worst plastics only where needed
- Bag manufacture close to pharma production
- Recyclable plastics availability: by demand or law
- Examine the many EOL potentials for local geography
- Biodegradable, bio-sourced, bio-based, or bio-plastics

Post-use handling

- Second-use
- Polymer recycling
- Land fill (untreated)
- Grind, sterilize & landfill
- Proximity of post-use plant
- Pyrolytic liquid fuel generation
- Cold pyrolysis increasing utility
- Transesterification to monomers
- Enzymatic-based depolymerization
- Incinerate with on-site power generation
- De-polymerize to re-usable plastic monomer
- Convert to re-purposed plastic boards/pallets`
- Reduce to C, H and O: re-synthesize monomer

Many ways of organizing / labeling approaches

- Structure, polymer, monomer, chemical, energy
- Mechanical, carbon and monomer
- Upcycling, recycling, downcycling
- Physical, chemical and elemental
- Primary, secondary and tertiary
- Reuse, repurpose and recycle
- Structure, material and energy

BIOPROCESS TECHNICAL

The Green Imperative

Part One: Life Cycle Assessment and Sustainability for Single-Use Technologies in the Biopharmaceutical Industry

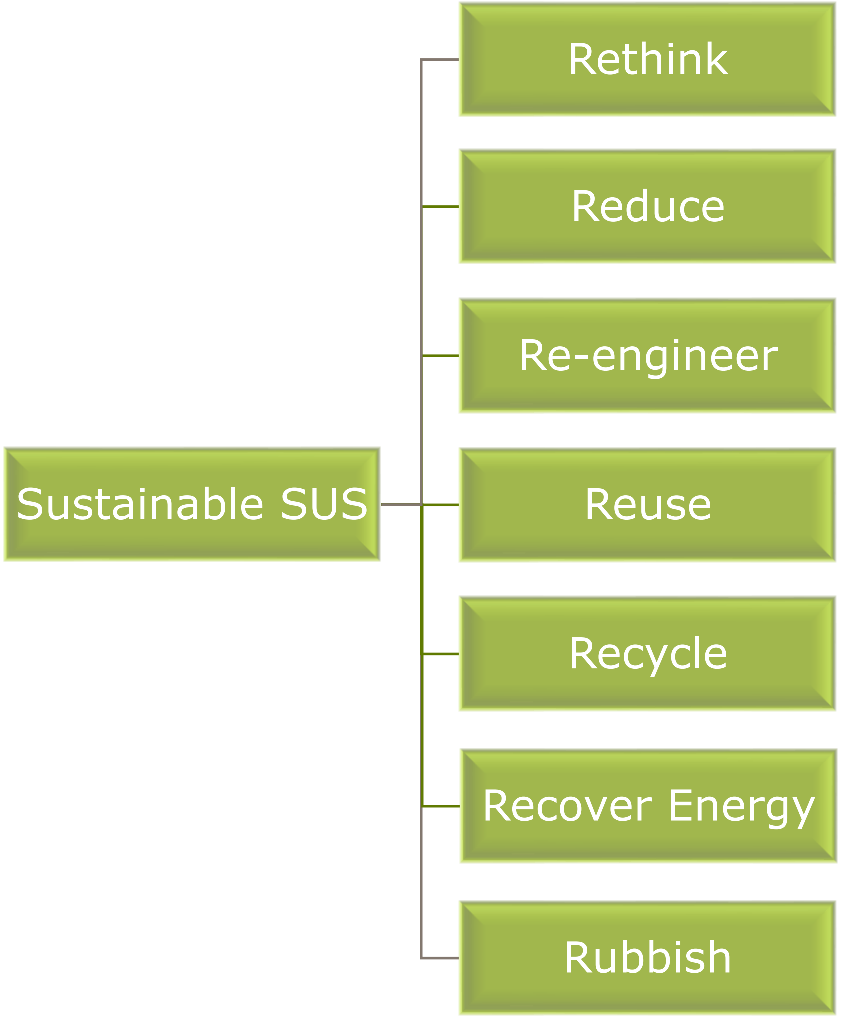
Magali Barbaroux, Brian Horowski, Sade Mokuolu, Mark Petrich, and William Whitford; with the BPSA Sustainability Subcommittee and Bill Flanagan

Much has changed since large-scale single-use biomanufacturing equipment was introduced some 15 years ago. Since then, these materials have become accepted and established in production and downstream bioprocessing. Concerns about the environmental impact of single-use (SU) biomanufacturing equipment have become more prevalent as our environmental awareness has increased and related concerns have become more urgent (1). For example, many recommendations and even laws have emerged regarding plastic convenience

The seven Rs

Rethink, reduce, re-engineer, reuse, recycle, recover energy, rubbish

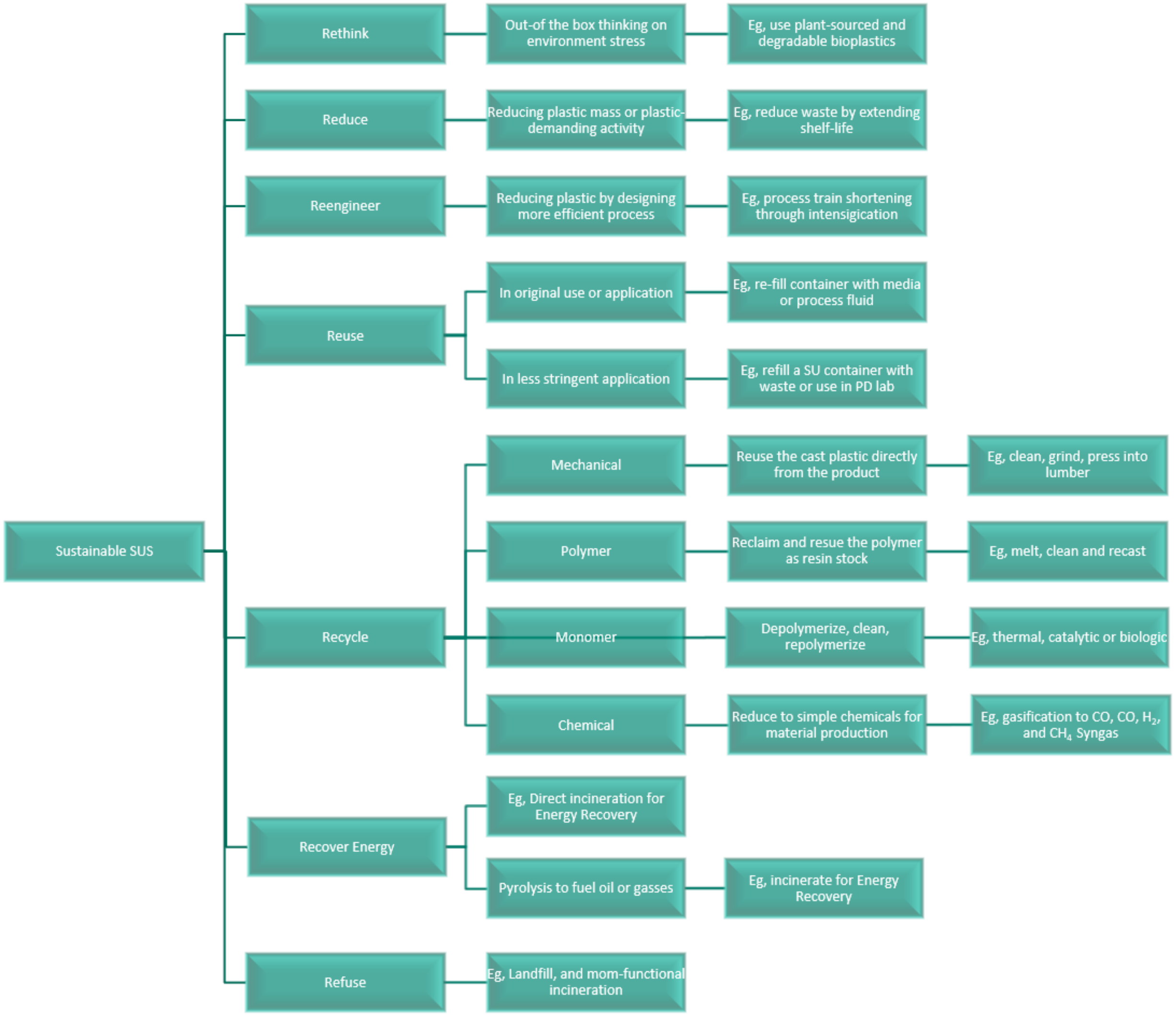
From new materials, to engineering and design, to post-use handling ("recycling" or "end-of-life")



The seven Rs

Each approach is currently studied

Some now commercially provided



The seven Rs

Rethink

E.g., use bioplastics for resin

Reduce

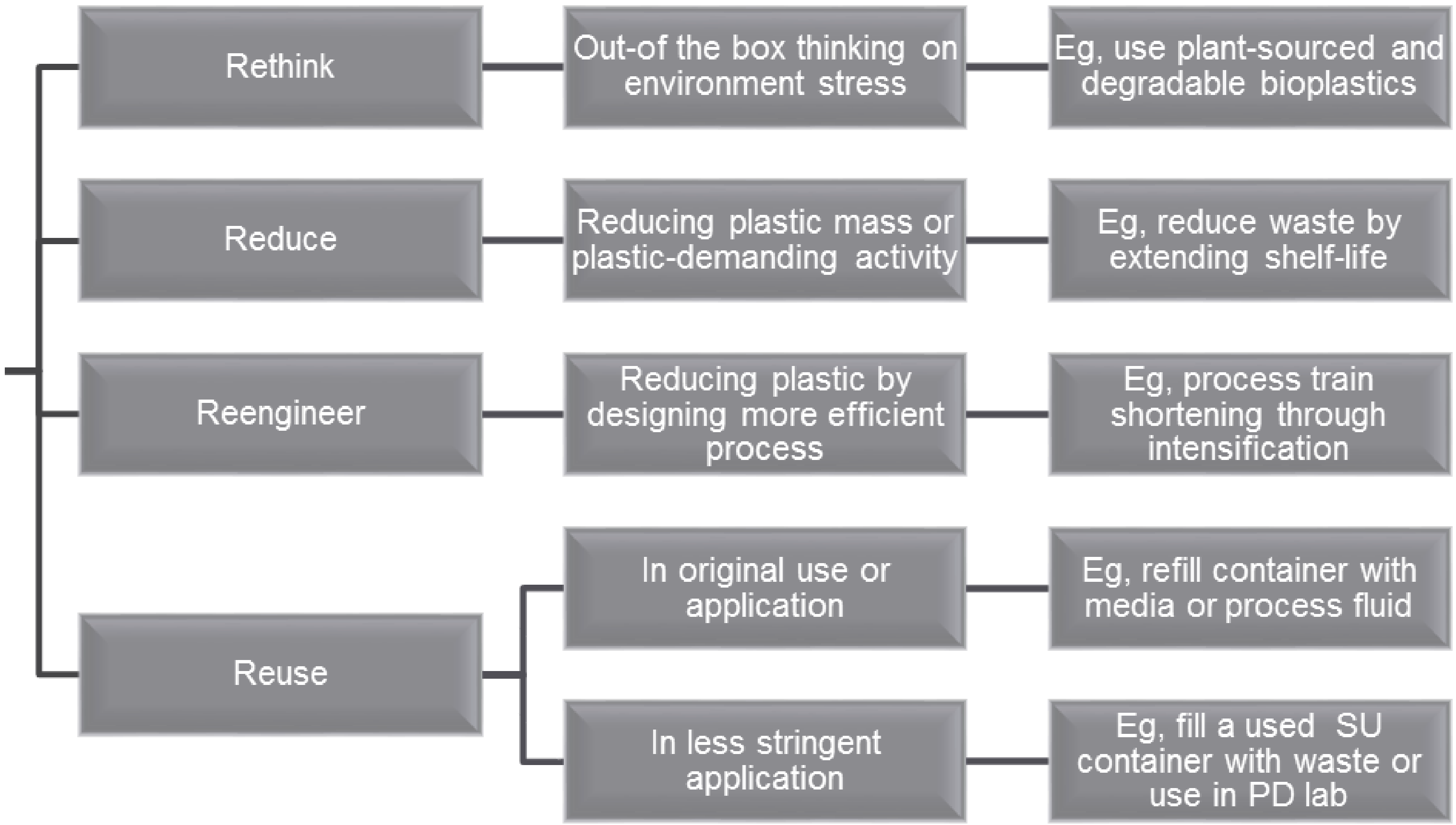
E.g., use less plastic mass or plastic-dependent activity

Reengineer

E.g., process intensification to increase plastic efficiency

Reuse

E.g., use again in same, or in a less stringent, application



The seven Rs

Recycle

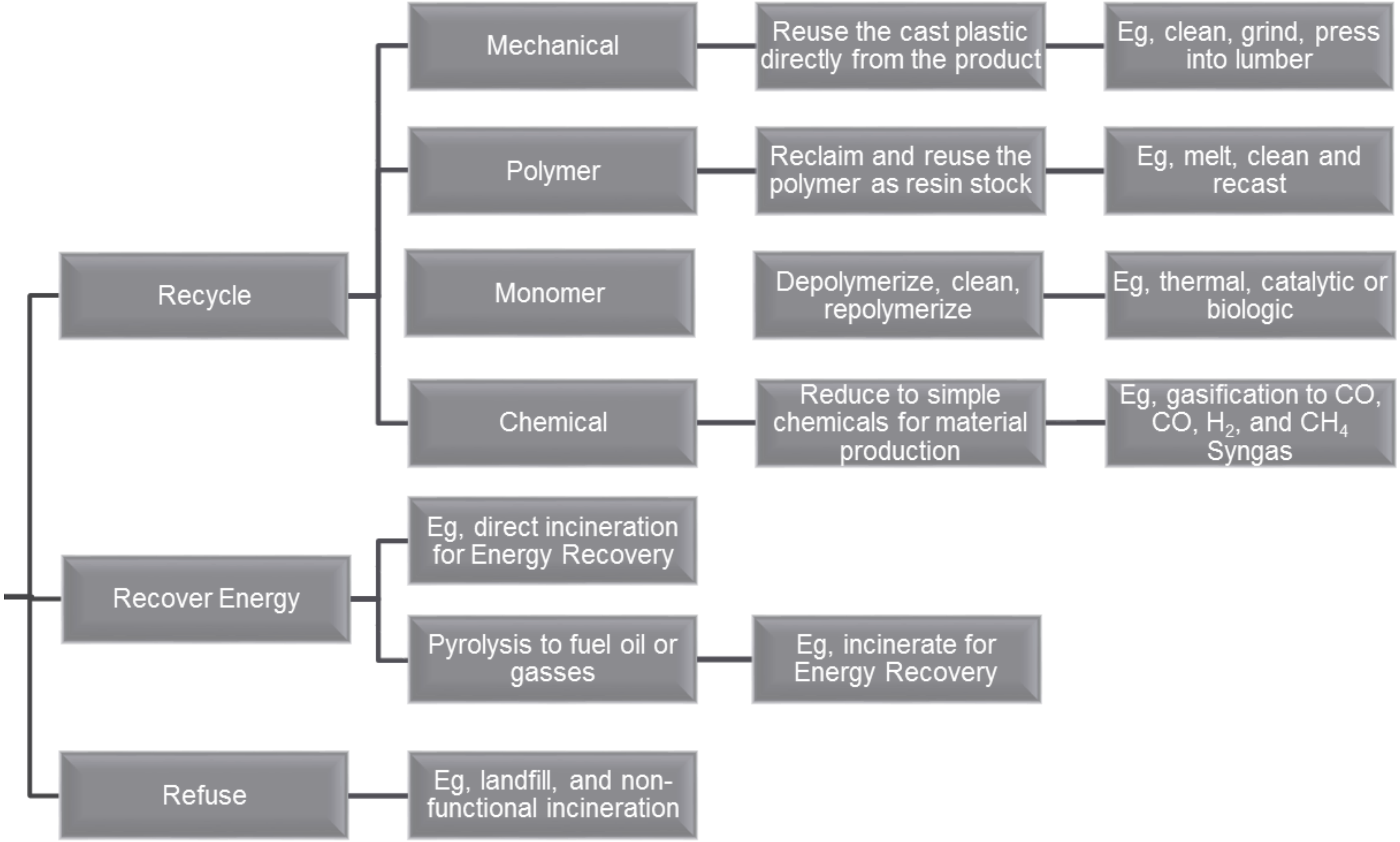
- Mechanical, polymer, monomer, chemical

Recover energy

- Incineration, pyrolysis

Refuse

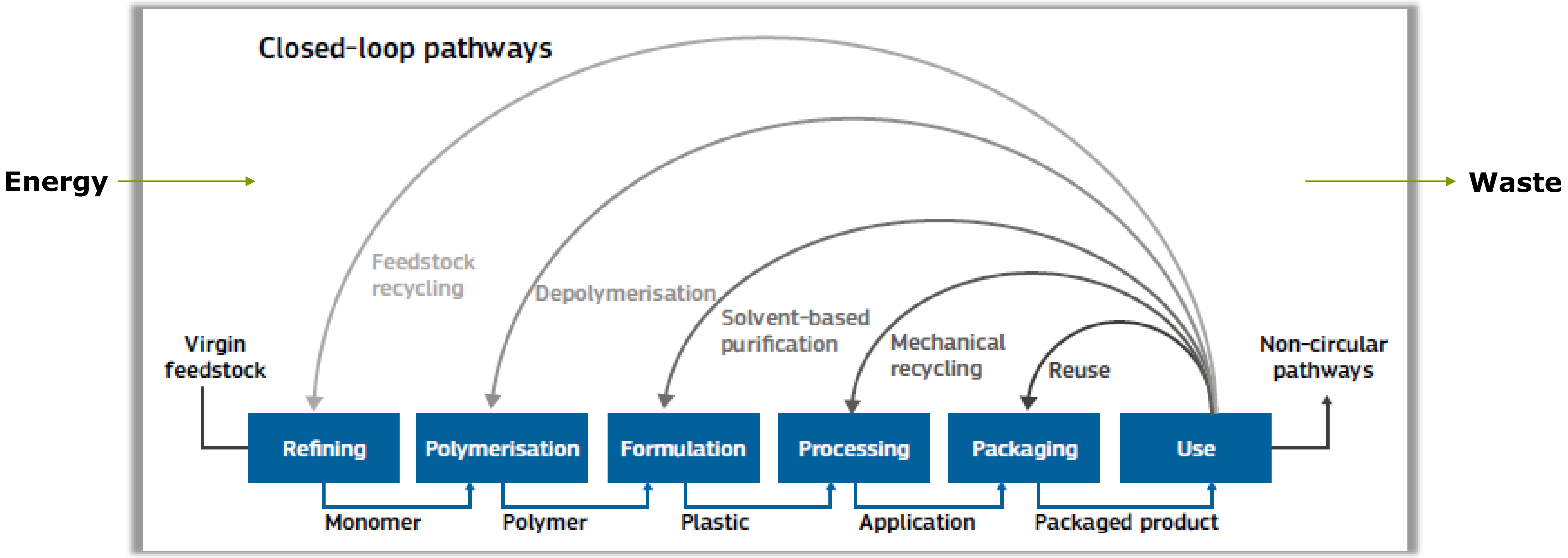
- Landfill or non-functional incineration



Many approaches, chemistries and pathways

Economy	*Approach*	*Post-use Technology*	*Example or Definition*
Circular	Plastic Renewal	Petrochemical reuse	Gasification to syngas and used as feedstock for monomer production
		Monomer reuse	Catalyzed glycolysis of PET to BHET for re-polymerization to PET resin
	Carbon Renewal	Polymer reuse	Cleaned, liquified and filtered polymer condensed to plastic resin stock
		Mechanical reuse	Processed, ground plastic casting formed into shipping pallets or lumber
Linear	Disposal	Landfill	Transport of raw or processed waste to either local or centralized landfill
	Re-, Up-, or Down-cycle. Repurpose	Product reuse	Post-use application of product in the very same functions or activities
		Product new use	Post-use application of product in new, higher or less stringent function
		Decomposition to mixed petrochemicals	Pyrolysis to porous (activated) carbon and terminal consumption in use
	Energy Recycle	Grind and incinerate	Catalyzed incineration to produce steam for use in electricity generation
		Decomposition to mixed oligomers	Catalyzed pyrolysis to hydrocarbon oil and terminally consumed as fuel

Even "circular" has degrees of sustainability



Adapted from BPSA, Engineering for Sustainability in Single-Use Technologies, BPI, *In Press* 2020

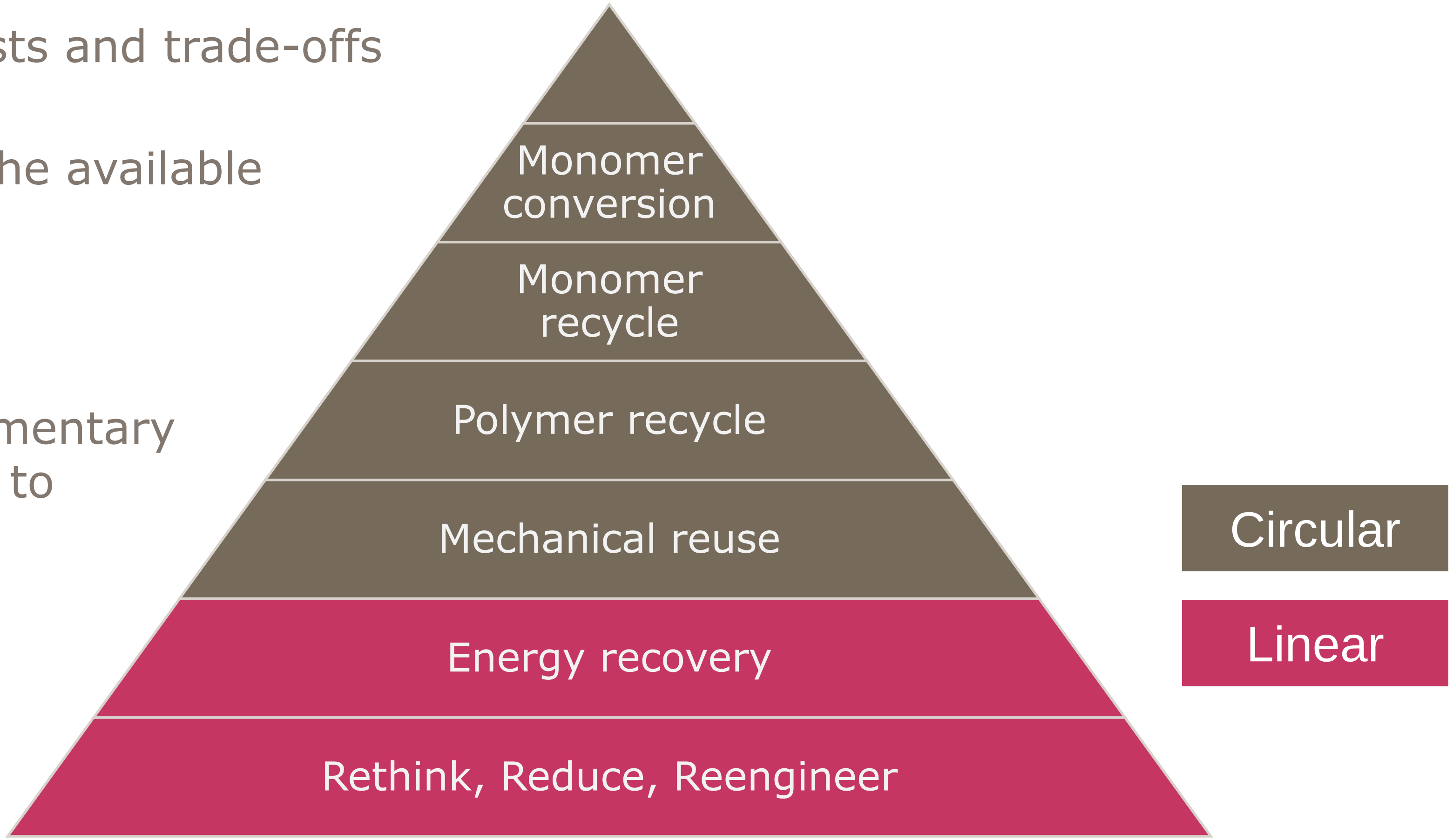
Possible sustainability hierarchy

Considering many long-term costs and trade-offs

Reflects an ideal, we must use the available

"Recycling technics are complementary and should be used as toolbox to reprocess any plastic waste."

Magali Barbaroux
Corporate Research Sartorius



New end-of-life capabilities

DPS

Automation provides rapid sorting

- Multiple sensor types provide rich data
- *Artificial Intelligence* provides computer vision
- Autonomous robots distribute and organize waste

Courtesy AMP Robotics
WWW . https://www.amprobotics.com/

ZDNet
VIDEOS WINDOWS 10 ENTERPRISE SOFTWARE

Recycling is broken. Can these robots help?

We're in the middle of a full-fledged international recycling crisis.

By Greg Nichols for Robotics | May 15, 2019 -- 11:00 GMT (04:00 PDT) | Topic: Robotics

***AMP Robotics** is another example of a company combining robotics, machine vision, and AI to make recycling faster and cheaper, raising the possibility that we can onshore our waste disposal.*

With permission: Greg Nichols for Robotics | May 15, 2019
https://www.zdnet.com/article/recycling-is-broken-these-robots-can-help/

Conclusion

Sustainable SU post-use options

1

Science-based and life-cycle approaches provide accuracy

2

Chemistries and options are not generally understood

3

There is much progress in the field currently occurring

4

Many circular chemistry options theoretically available

5

Few options are available now, but are in development

Thank you

Bill Whitford

Strategic Solutions Leader

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