

Industrial green chemistry & technology

Design and development strategies

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Agenda

- Green chemistry and engineering
- GCT platforms and innovations
- Integrating GCT into industrial practices
- GCT and business strategies
- Promise of renewables
- GCT directions
- Conclusion

Green chemistry & engineering




- “An approach to addressing the environmental consequences of chemical products or processes at the design stage”
 - It utilizes a set of principles to reduce or eliminate the use or generation of hazardous substances at design, manufacturing and application stage.
 - A methodology that changes the intrinsic nature of process or product to make it benign
 - Heralded a new phase in chemical industry that took shape in early 90's

Drivers for green chemistry

- Bhopal incident - a key driver
- High cost of EHS management systems
- Build up of regulatory and community pressures
- Pressures to rationalize R&D / manufacturing
- Realization of economic gains
- Promise of renewables, catalysis, etc.
- Innovations in manufacturing practices, R&D, automation, unit processes and operations...
- Emergence of new technologies like MRT, enzyme and biocatalysis

Environmental waste (the E-factor)

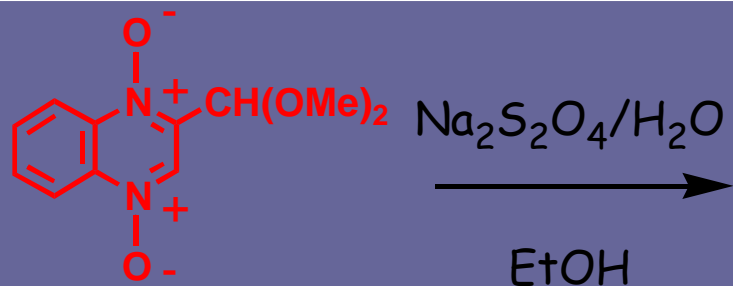
- The amount of waste per kilogram of product (“kilos in/kilos out”) varies across chemical industry sectors.

	Industry Sector	Annual Product Tonnage	E – factor
	Bulk chemicals	$10^4 - 10^6$	1 - 5
	Fine chemicals	$10^2 - 10^4$	5 - 50
	Pharmaceuticals	$10 - 10^3$	25 - 100

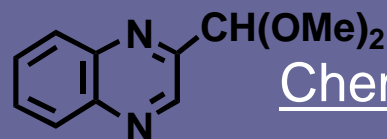
R&D philosophy aligned with green chemistry principles

	Thinking Environmentally (Reduced environmental burden)	Thinking Economically (Reduced cost)
Atom Economy	Minimal by-product formation	More from less—incorporate total value of materials
Solvent Reduction	Less solvent waste	Higher throughput, less energy
Reagent Optimization	Catalytic, low stoichiometry, recyclable reagents minimize usage	Higher efficiency—higher selectivities
Convergency	Increased process efficiency	Higher efficiency—fewer operations
Energy Reduction	Power generation, transport, and use	Reflects increased efficiency, shorter process, mild conditions
<i>In situ</i> Analysis	Reduced possibility for exposure or release to the environment	Real-time data increased throughput and process efficiency, fewer reworks
Safety	Non-hazardous materials reduce risk of exposure, release, explosions, and fires	Worker safety and reduced downtime, Reduced time on special control measures

Chemical & Biocatalytic Routes to QCA

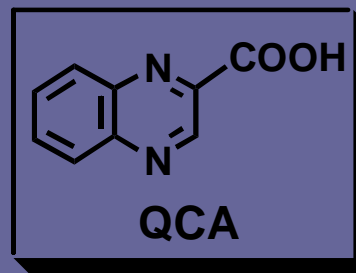
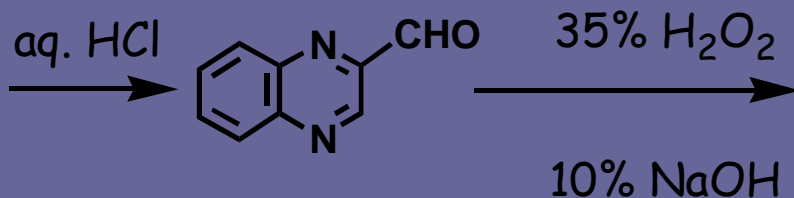


di-N-oxide



Chemical Route

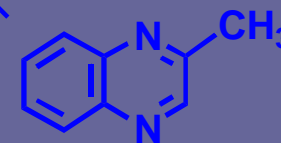
- 3 steps, 35% yield
- Di-N-oxide: mutagenic & high energy intermediate



Biocatalytic Route

- 1 step (3 enzyme reactions), 86% yield
- Aqueous reaction at 28°C

Pseudomonas putida
whole cells



2-Methylquinoxaline

Chemical & biocatalytic process comparison

Raw materials for 1 kg QCA

Chemical Process		<i>P. putida</i> Process	
di- <i>N</i> -oxide	3.9 kg	2-methylquinoxaline	0.97 kg
Na ₂ S ₂ O ₄	5.7 kg	benzyl alcohol	2.9 L
35% H ₂ O ₂	6.5 L	<i>p</i> -xylene	0.9 L
4N HCl	13.6 L	4N HCl	3.8 L
10% NaOH	11.7 L	10% NaOH	1.7 L
chloroform	142 L	inorganic salts	0.75 kg
<i>N,N</i> -dimethylacetamide	36 L	trace elements	0.005 kg
ethanol	18 L	H ₂ O	79 L

- Biocatalytic route avoids hazardous di-*N*-oxide and uses 4 less starting material
- Reduced organic solvent consumption for biocatalytic route (3.8 L/kg QCA) vs. chemical process (196 L/kg QCA)

GCT platforms and innovations



J.H.Clark in Green Separation Process, Wiley – VCH, 2005

Biotechnology

2009	Eastman Chemical Company	Immobilized enzymes, such as lipase, used to make a variety of esters for cosmetics and personal care products
2008	Metabolix, Inc.	Spinetoram, a new spinosyn insecticide that is more effective than a related pesticide, spinosad, which was a 1999 Challenge <u>Award</u> winner, but maintains spinosad's low toxicity to mammals and other non-target species
2006	Codexis, Inc.	Directed evolution of biocatalysts to produce the key chiral intermediate for Lipitor®

www.usepa.gov/greenchemistry

Biotechnology (contd...)

2005	Archer Daniels Midland Company	Novozymes Enzymes used to produce low <i>trans</i> fats and oils for foods
2005	Dow AgroSciences LLC	Bioplastics (polyhydroxyalkanoates) made by genetically engineered organisms
2004	Bristol-Myers Squibb Company	Plant cell fermentation used to make paclitaxel, the active ingredient in the drug Taxol®
2004	Buckman Labs International, Inc.	Enzyme used to control sticky contaminants during paper recycling

Polymer

2009	The Procter & Gamble Co; Cook Composites & Polymers Co.	Chempol® MPS alkyd polymer resins used in conjunction with Sefose® sucrose esters to reformulate conventional oil-based paints
2007	Cargill, Incorporated	Polyurethane foams can now be made with biobased BiOH™ polyols instead of petroleum-based polyols
2006	S.C. Johnson & Son, Inc.	Greenlist™ Process guided the replacement of polyvinylidene chloride with polyethylene in Saran Wrap®
2005	BASF Corporation	Primer for automotive refinishing; applied as a urethane acrylate oligomer that crosslinks by UV light into the cured film

Biopolymers

2008	Battelle	Biobased polyesters, polyamides, and polyurethanes resins made from soy oil and protein along with corn carbohydrate are components of toner for photocopying and printing
2007	Metabolix, Inc.	Bioplastics (polyhydroxyalkanoates) made by genetically engineered organisms

Renewables

2009	Virent Energy Systems, Inc.	Sugar, starch, or cellulose from plants used in the BioForming® process to make gasoline, diesel, or jet fuel
2007	Prof. Kaichang Li, Oregon State Univ.; Columbia Forest Products; and Hercules Inc.	Soy-based adhesive replaces urea-formaldehyde resin for plywood and other wood composites

Safer chemicals

2008	SiGNa Chemistry, Inc.	Alkali metals encapsulated in porous metal oxides retain their high reactivity, but are not dangerous to store or handle
2006	Arkon Consultants, NuPro Technologies, Inc.	Safer solvents and solvent recovery system for flexographic printing
2005	Engelhard Corporation (now BASF Corporation)	Rightfit™ azo pigments contain calcium, strontium, or barium, have low potential toxicity, low migration rates, and are made in aqueous medium; traditional pigments contain heavy metals (lead, chromium (IV), cadmium) and use polychlorinated intermediates and organic solvents

Solvent technologies

2007	NovaSterilis Inc.	Supercritical carbon dioxide and a peroxide used for sterilization of delicate biological materials
2004	Profs C. A. Eckert and C. L. Liotta, Georgia Inst. of Tech.	Tunable solvents, particularly supercritical carbon dioxide (scCO ₂), near critical water, and CO ₂ -expanded liquids, couple reactions and separations, replacing organic solvents and minimizing waste
2002	SC Fluids, Inc.	Supercritical CO ₂ removes photoresist from semiconductor wafers, replacing hazardous solvents and corrosive chemicals

Synthetic processes

2005	Merck & Co., Inc.	A convergent synthesis of aprepitant, the active ingredient in Emend®, with half the synthetic steps, almost double the yield, and a reduction of nearly 80% in both raw materials and waste
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Integrating GCT into industrial practice

A. Leveraging green chemistry principles

- i. Alternative reaction media
- ii. Alternative reaction conditions
- iii. Alternative chemical design
- iv. Alternative reaction techniques

i. Alternative reaction media: Phosgene replacement

- DuPont : isocyanates by direct carbonylation of amines with carbon monoxide
- Monsanto Chemical Company : Dehydrating agent (O-sulfobenzoic acid anhydride) for highly selective conversion of amines
- Asahi Chemical Co: Polycarbonates by molten state reaction of Bisphenol A and diphenylcarbonate
- Enichem Chemical Company: Direct carbonylation of methanol using carbon monoxide, eliminating use of phosgene.

ii. Alternative reaction conditions

- Bio catalysis: revolutionizing synthetic processes
 - Use of Escherichia coli to convert D-Glucose to adipic acid eliminated the need for benzene in phenol manufacture
 - Bio transformation of glucose into 3-Dehydroshikimate (DHS), building block for adipic acid, catechol etc
 - DuPont's bio-catalytic process for glyoxylic acid by enzymatic oxidation of glycolic acid using whole cell of a recombinant methylotropic yeast. Conventional process involved nitric acid oxidation of acetaldehyde
 - Lonza's process for 5-methylpiperazine-2-carboxylic acid
 - DSM's process for cephalosporins

ii. Alternative reaction conditions (contd.)

- Zeolite catalysts
- Pd catalysis
 - Shell: single step route to methylmethacrylate by Pd catalysed methoxycarbonylation of methylacetylene
 - Hoffman La Roche: Lazabemide synthesis from 2,5-dichloropyridine replaces 8 step route from 2-methyl-5-ethylpyridine
- Non conventional catalyst systems
 - Monsanto: P-nitroaniline, interesting example of how halogen mediated substitution was replaced by a process involving the substrate

iii. Alternative chemical design

- Manipulation of molecular structure, functional groups, and stereochemistry
 - Retention of desired chemical properties and efficacy of use, while eliminating undesirable properties
- DuPont's just-in-time (JIT) process for MIC
 - Masked synthons and improved catalytic oxidative-dehydrogenation
 - Allows production and conversion of MIC to the final agricultural chemical product in situ
 - Eliminates large inventories

iv. Alternative reaction techniques

■ Solid state

- Aqueous-based, solid state, and neat reactions (solvent-less)
 - Decrease inhalation exposures and potential ambient emissions.

■ Supercritical fluids

- Replacement reaction media for volatile organic solvents

B. Leveraging green engineering principles

- Energy efficiency
 - Eastman Chemical's integrated esterification of methanol with acetic acid and distillation of methyl acetate in a single vessel with a liquid-phase catalyst
- Safer processes
 - Polimeri Europa (formerly Enichem) pioneered the development of dimethylcarbonate (DMC) by methanol oxycarbonylation

... Green engineering principles (contd.)

■ Process intensification (PI)

- Replace large, expensive and inefficient equipment by smaller, more efficient and inexpensive plant by combining multiple operations in fewer apparatus
- The DSM Urea 2000Plus process is a more recent illustration of PI as a "size reducer"

■ Process integration

- Pinch analysis
- Knowledge based approaches
- Numerical and graphical optimization approaches

... Green engineering principles (contd.)

■ Process simulation

■ Waste reduction algorithm (WAR)

- Accounting method for pollution generation that introduces a yardstick for comparing pollution generation of different processes
- Systematic design model to determine the pollution index of a product (*defined as the amount of waste produced per unit mass of product*)

■ Environmentally acceptable reaction [EAR]

- Mathematical tool to systematically synthesize environmentally acceptable reaction sequences

... Green engineering principles (contd.)

■ Safer process

- The catalytic production of propylene oxide with H₂O₂ as an alternative to chlorine and water as the sole final by-product is under development in these processes
 - UHDE and Degussa: fixed bed reactor, licensed to SASOL
 - Sumitomo: oxidation with cumylperoxide
 - Nippon Shokubai: 99% selectivity with silicotungstates

GCT and business strategies

GCT and business strategies

- Dow: **Introduced solutions-based business models**
 - Transition from product-focused approach to "product-agnostic" model - marketing formulation and application expertise
- BASF: **Adopted greater precision in business processes**
 - Pricing, marketing, customer management, and product development
- Rohm and Haas: **Developed markets for new platforms**
 - Biocides, personal care ingredients, and ion-exchange resins

GCT orientation and business strategies

- CIBA: **Reorganised its R&D into product areas**
 - Protection and stabilizing chemistries, color components, polymerization and curing chemicals, interface and rheology additives, paper and coating chemicals
- Clariant: **combined product and service orientation**
 - Textile, leather, and paper chemicals; Pigments and additives; Functional chemicals; Color and color additives, master batches
- FMC: **Exploring new application platforms**
 - Exploring new applications in energy, electronics, and other industrial markets

Lab to market place ...

■ Adhesives

- Light weighting through material substitutions
- Extreme condition performance
- Auto, aero space

■ Detergents

- Biodegradable products - Henkel

■ Coatings

- Low environmental foot print
- Super solid ultra low emission products - DuPont
- Fundamental molecular engineering

Lab to market place...

■ Fibres

- Biopolymers, nonwoven from nanofibres, micro-encapsulation

■ Colorants

- DyStar's Levafix CA reactive dyes... over 90% fixation
- Ciba: Cibacron S dyes "thrice-reactive" chemistry
- Clariant: Drimarene HF reactive dyes [no halogen bound]

■ Construction chemicals

- New chemistries in concrete admixtures - Polycarboxylates
 - Nippon Shokubai, Degussa, WR Grace, Sika



Raw materials → Manufacture → Distribution → Use → Disposal/recycle

- Lightweight plastics and composites
- Paint to increase durability
- Improved efficiency seals
- Specialty pigments

- Antifouling paints to reduce marine pollution and fuel consumption

- Adhesives which aid disassembly

- Lower VOC paints
- Biodegradable metal working fluids
- Specialty adhesives
- Non wovens

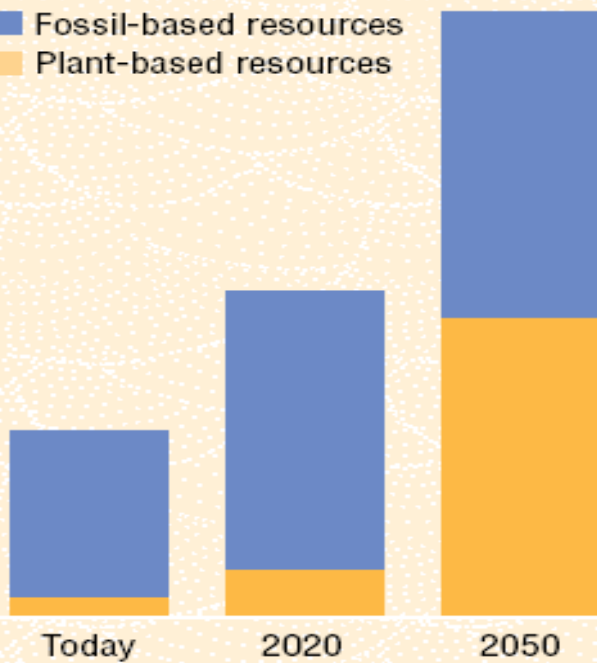
- Lubricants and fuel additives to improve fuel economy and emissions
- Exhaust catalysts
- Biofuels
- Fuel cells and other new power units

Innovation tools

- New chemistries & engineering
 - Innovative chemical/bio/catalytic/ nano/ MRT
 - Process design and development
 - Adoption of GCEP
- Supply chain optimization
 - Partnering for product development
- Operational excellence
 - Lower manufacturing variability
 - Agile manufacturing systems
 - Benchmarking

Promise of renewables

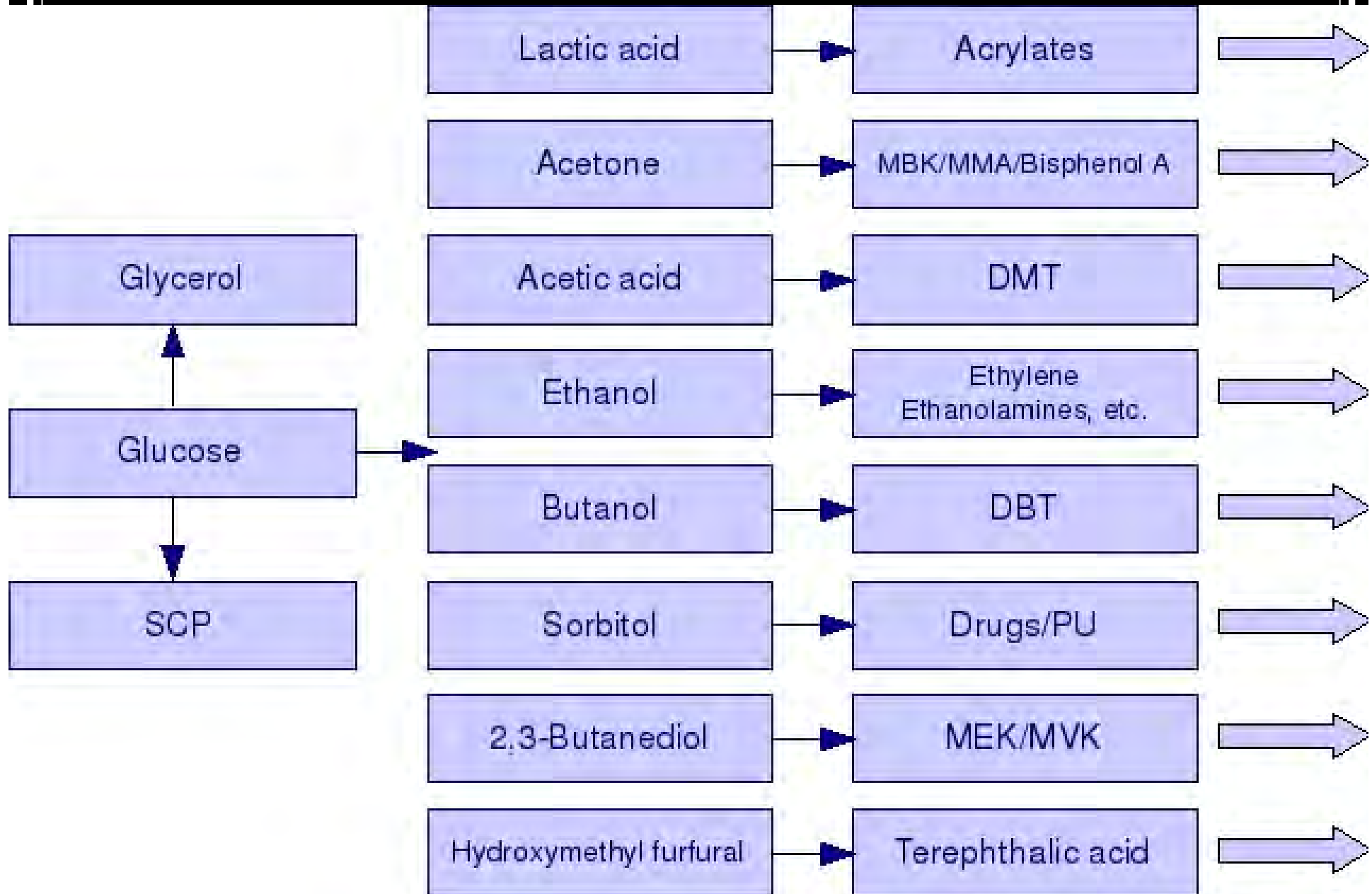
■ Fossil-based resources
■ Plant-based resources



Chemicals from renewables

- High-margin biopharmaceuticals and bioveterinary products
- High-value chemical specialties
- Moderate to low-value fermentation bulk chemicals
- Minimum demand critical
- On a learning curve
- Need to enable greater functionality and performance
- Comparative economics vis a vis petrochemical technologies
- Cost advantages needed
 - Process design
 - Capital investment
 - Social and customer value

Chemicals from renewables



Chemicals from renewables

Chemicals	Source	Derivatives
Glycerin	Biodiesel	PG [Dow-Cargill] Epichlorohydrin [Dow-Solvay]
Lactic acid	Cellulose to ethanol	Polylactic acid, ethyl lactate
Methacrylate monomers	Cellulose to ethanol	Acrylic polymers [RH-Ceres]
Levulinic acid	Cellulose to ethanol	Methyl THF
1,3 Propane diol	Cellulose to ethanol	Polyesters
Succinic acid	Cellulose to ethanol	1,4-butaendiol, gamma buytrolactone , NMP
Acetic acid	Corn starch to ethanol	Vinyl acetate monomer, esters
13, butanediol	Corn starch to ethanol	Gamma butyrolactone
Citric acid	Corn starch to ethanol	Food ingredients

Concept to market realities

- Dupont –Genencor: 1,3-propane diol for PTT
- DuPont: Propylene glycol (3G) from corn-derived glucose
- Dow Cargill: Polylactic plant in USA
- BASF, Degussa and Dow – Bio routes for Vitamins, Amino acids
- MBI : Succinic acid -1,4-butane diol, THF, L-Lysine, Adipic acid
- Nitto –Acrylo nitrile to Acrylamide
- Dow-Crystalsev, Brazil: 350000 tpa PE from sugarcane 2011
- Chinese JV: 150000 tpa Epichlorohydrin from glycerine 2010
- DSM-Roquette: Succinic acid from starch, France, 2011

Concept to market realities

- Ethanol (C2)
 - Lactic acid (C3)
 - Succinic acid (C4)
 - Citric acid (C6)
-
- Will these form the basic feedstocks for the chemical industry?

Renewables: growing concerns

- Feedstocks generation: social, economic, new technologies, land use
- Bio process technology: nascent
- Prices: linked to prices for alternative uses
- Policy: food vs fuel vs chemical feedstocks
- Financing: low response from banks/ PC
- Sustainability criteria: not in place

Green chemistry & technology directions

GCT directions

■ GCT drivers

- Non competitive feed stocks
- Environmental mandates
- Global market shifts
- Alternative feed stocks: renewables
- Shift in business structures and processes
- Improved capability to design GCT platforms
- Adaptability to market and regulatory demands

GCT: Strategy focus

- Water reuse
- Reaction engineering
- Biotechnology
- Chemical separations
- In-process waste reduction
- Agile manufacturing
- Inherently safer processes
- Non-conventional feedstocks
- Plant design and optimization
- Process engineering
- Solids processing

GCT: Operational focus

- Reduced manufacturing variability
- Environmental footprint
- Agile manufacturing systems (quick changes on several time scales)
- Manufacturing reconfiguration
- Integration and interconnectivity of production into business operations

GCT: Future directions

- Wider use of oxygen as a selective oxidant
- Renewable feedstocks: biomass, starch, cellulose
- Enantioselective catalysis
- Wider use of enzymes in chemicals production
- More-energy-efficient chemical syntheses
- Photocatalysis with visible light

GCT: Taking green innovation to markets

- Benchmarking, standards and norm settings
- Technology partnering and alliance forming
- Licensing and contracting
- Technology-supply chain linkages
- Technology-economics
- Technology selection and transfer
- Funding innovation
- Assessment of technological options

GCT: Game changing platforms

- Nanotechnology
- Advanced catalysis
- Biocatalytic synthesis
- Biochemical routes
- Biodegradable products
- Conductive polymers
- Fuel cells
- Micromachining technology

Conclusion

- GCT, a bench level tool leading to value creation
- Companies learning to operate and compete in diverse regulatory environments
- Tighter legislative controls
- Process and product protocols
- Maximizing innovations to meet sustainability demands

Thank you!

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