



Learning lessons from measuring Green Chemistry performance

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Sustainability & Environment

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Our flagship products: Pharmaceuticals

ADVAIR DISKUS[®] 100/50
(fluticasone propionate 100 mcg and salmeterol 50 mcg inhalation powder)

**SERETIDE[™]**
salmeterol/fluticasone propionate

ONCE DAILY
Arixtra[®]
(fondaparinux sodium) for injection

0.5 mg/Once Daily
AVODART[®]
(lutasteride)
Soft Gelatin Capsules

LOVAZA[®]
omega-3-acid ethyl esters

**Cervarix[®]**
Human Papillomavirus Vaccine Types 16 and 18
(Recombinant, adjuvanted, adsorbed)

Rotarix[™]
rotavirus vaccine

Tykerb[®]
(lapatinib)

Tyverb[®]
Lapatinib

What is corporate responsibility?

Key Facts 2009

Community investment
valued at

£163m



1bn

Supplied 1.4 billion vaccine doses globally
for prevention of serious diseases, one
billion for use in developing countries

45%

Reduced the prices of 11 patented GSK
medicines by an average of 45% to improve
access in Least Developed Countries

12

R&D investment
into 12 diseases
of particular
importance for the
developing world



£4.1bn

Invested £4.1 billion and 15,000 people
employed in R&D

15%

GSK endorsed the United Nations CEO
Water Mandate in 2009 and we have
reduced water use by more than 15 per
cent since 2006

56,000

Savings of 56,000 tonnes of CO₂ equivalent emissions annually
are expected from nearly 300 energy saving projects
completed in 2009

£50m

Together with Pfizer we launched
specialist HIV company ViiV Healthcare.
A new £50 million Positive Action for
Children Fund was announced in 2009.
ViiV Healthcare will make this available
over ten years to help prevent mother-to-
child transmission of HIV and to support
orphans and vulnerable children



472m

472 million anti-retrovirals shipped to the
developing world at preferential prices,
including 439 million supplied by generic
manufacturers licensed by GSK



Measuring 'Greenness'

Nappies – which are greener?



Washable

<http://www.littlelamb.co.uk/itemlist.php?clasrefr=products>



Disposable

<http://www.huggies.com>

Nappies: which are greener? Disposable or washable?



Women's
Environmental
Network

*Educating, empowering and informing women and men who care about the environment.
Campaigning on environment and health issues from a female perspective.*

Media Statement

19 May 2005

Environment Agency nappy report is seriously flawed

was **no significant**

difference between the majority of
products

Need objective measures of
greenness that are agreed by
the majority





What are we doing in GSK?

Focus on Mass Efficiency – set a target



$$\text{Mass Intensity} = \frac{\text{kg raw materials}}{\text{kg API}}$$

$$\text{Mass Efficiency} = \frac{1}{\text{Mass Intensity}} \%$$

FT.com COMPANIES **Pharmaceuticals**

Plans to cut d
back, Pharmaceuticals Cor

Published: November 15 2009 22:23 | Last updated: November 15 2009 22:23

GlaxoSmithKline has set a target to cut by two-thirds the waste generated by medicines production from levels that until recently required 100kg of raw materials for every 1kg of drug produced.

The UK-based pharmaceutical group aims by 2015 to cut waste in its factories around the world to 30kg for each 1kg of "active pharmaceutical ingredient" (API), compared with an average of 100kg in 2005.

Management
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instant market insight

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MONEY SUPPLY

He stressed that the 100:1 ratio of inputs to API was a typical average across the pharmaceutical industry, and below the levels of waste generated by other manufacturers, including those in industrial chemicals.

GSK set an initial target in 2005 to halve the waste from raw materials by 2010, and raised that recently as it got close to achieving the objective. Its renewed aim is cut to cut waste to less than one-third of those original levels within five years.

The reductions come through measures including changing and reducing the number of chemical steps required, cutting the volume of solvents, and switching to continuous manufacture of a single drug to remove the wastage involved in stopping, changing and restarting batches of different products.

R&D
will achieve a target of **2.5%** for transferred processes to GMS for pharmaceutical products launched from 2011 to 2015

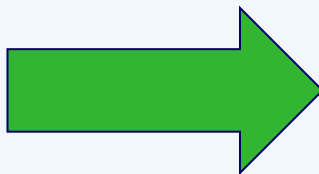
GMS
(working with R&D) will achieve a target of **3%** for pharmaceutical products launched from 2007 to 2012

Aspirational target of 5% Mass Efficiency by 2020

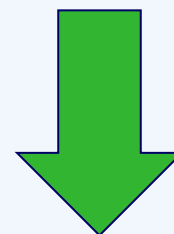
Green metrics – measure progress

Green Chemistry Metrics

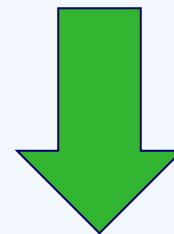
Collect
operational
metrics



Mass per kg/kg API
Process Water Mass kg/kg API
Materials of concern
Life cycle data (FLASC)



Benchmarking



Transparency

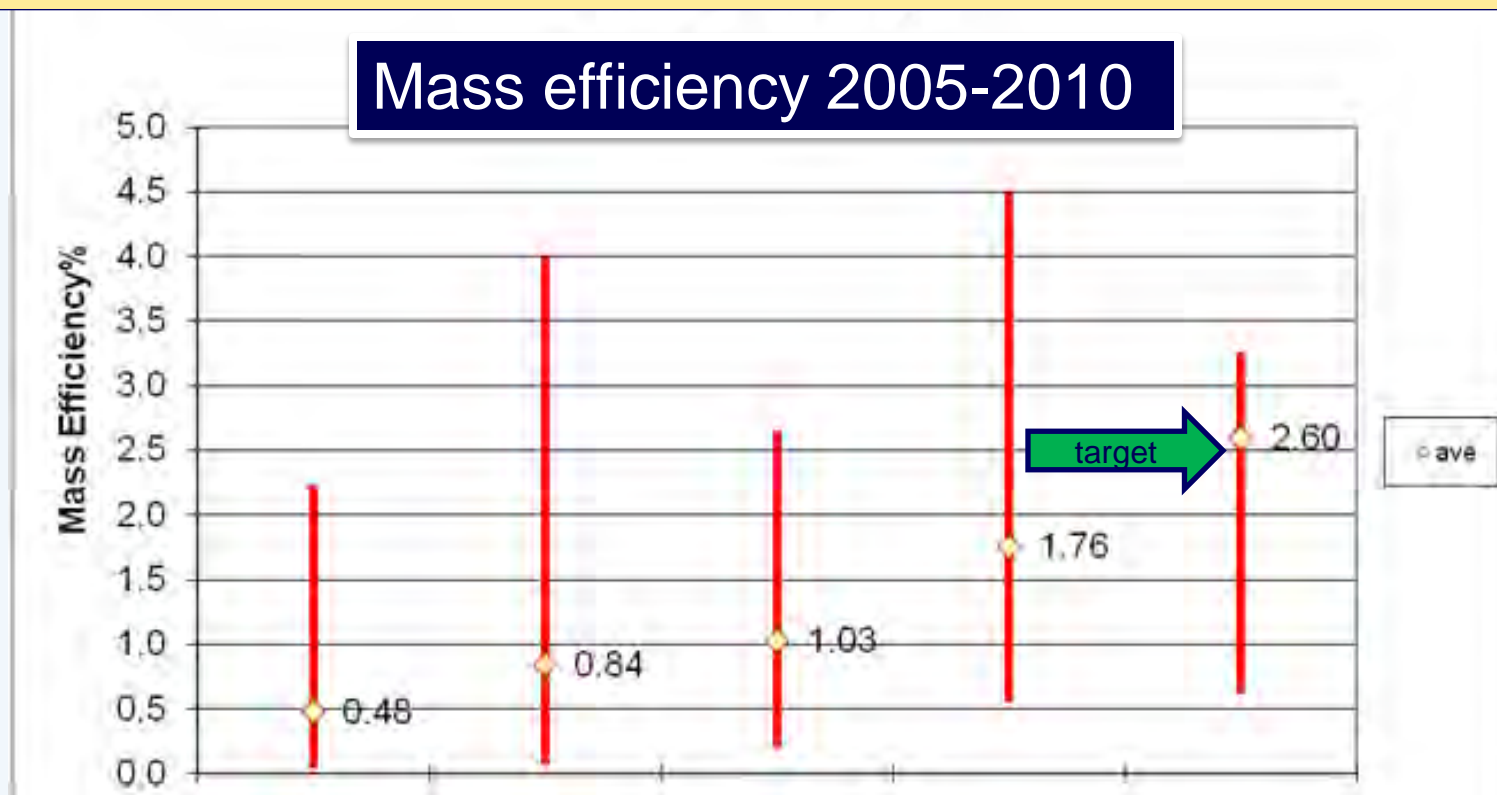


Mass efficiency – publish data



Mass Efficiency

R&D target is ME of 2.5% for average of the portfolio of transferred products starting from Registered Starting Materials including any demonstrated solvent recovery

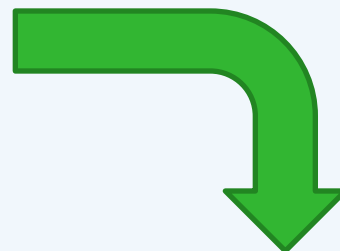
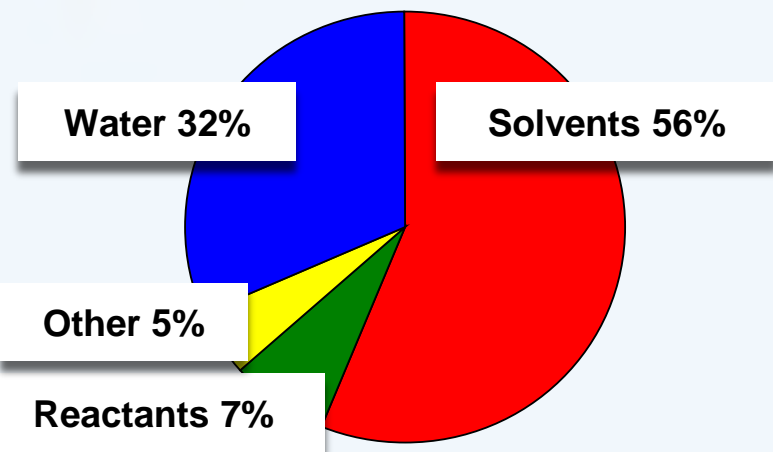


Pre-clinical



towards full scale commercialisation

Analyse the data - Solvents



Green Solvent Guidance

Composition by mass of types of material used to manufacture an API

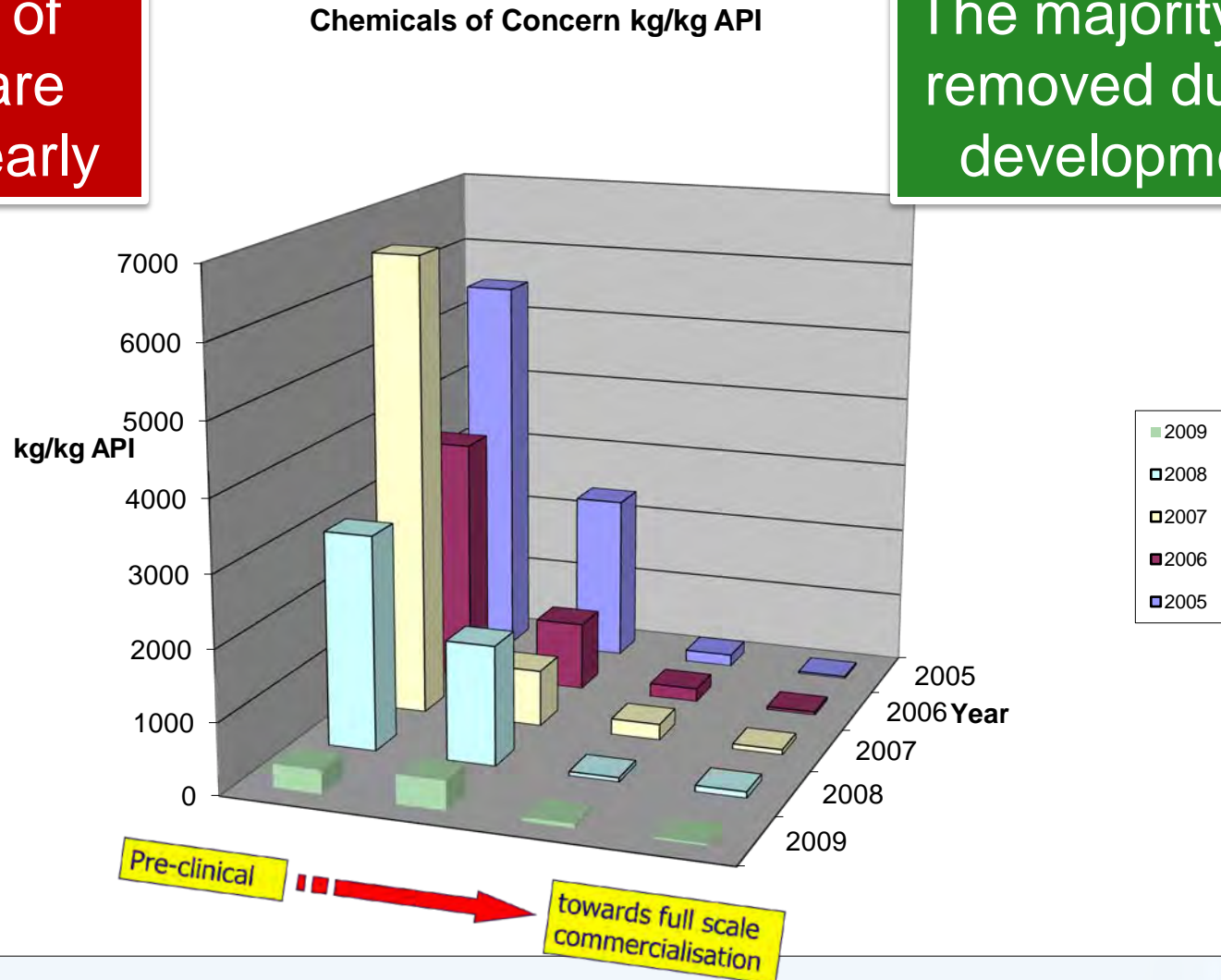
American Chemical Society Green Chemistry Institute
Pharmaceutical Roundtable Benchmarking 2006 & 2008

	Few issues (bp°C)	Some issues (bp°C)	Major issues
Chlorinated		...before using chlorinated solvents, have you considered TBME, isopropyl acetate, ethyl acetate or 2-Methyl THF?	Dichloromethane ** Carbon tetrachloride ** Chloroform ** 1,2-Dichloroethane **
Greenest Option	Water (100°C)		
Alcohols	1-Butanol (118°C) 2-Butanol (100°C)	Ethanol/IMS (78°C) t-Butanol (82°C) Methanol (65°C) 1-Propanol (97°C) 2-Propanol (82°C)	2-Methoxyethanol **
Esters	t-Butyl acetate (98°C) Isopropyl acetate (89°C) Propyl acetate (102°C)	Ethyl acetate (77°C) Methyl acetate (57°C)	
Ketones		Methyl isobutyl ketone (117°C) Acetone (56°C)	Methyl ethyl ketone
Aromatics		p-Xylene (138°C) Toluene ** (111°C)	Benzene **
Hydrocarbons		Isooctane (99°C) Cyclohexane (81°C) Heptane (98°C)	Petroleum spirit ** 2-Methylpentane Hexane
Ethers		t-Butyl methyl ether (55°C) 2-Methyl THF (76°C) Cyclopentyl methyl ether (106°C)	1,4-Dioxane ** 1,2-Dimethoxyethane ** Tetrahydrofuran Diethyl ether Diisopropyl ether **
Dipolar aprotics		Dimethyl sulfoxide (189°C)	Dimethyl formamide ** N-Methyl pyrrolidone ** N-Methyl formamide ** Dimethyl acetamide ** Acetonitrile

Analyse the data - Materials of Concern

Materials of concern are identified early

The majority are removed during development

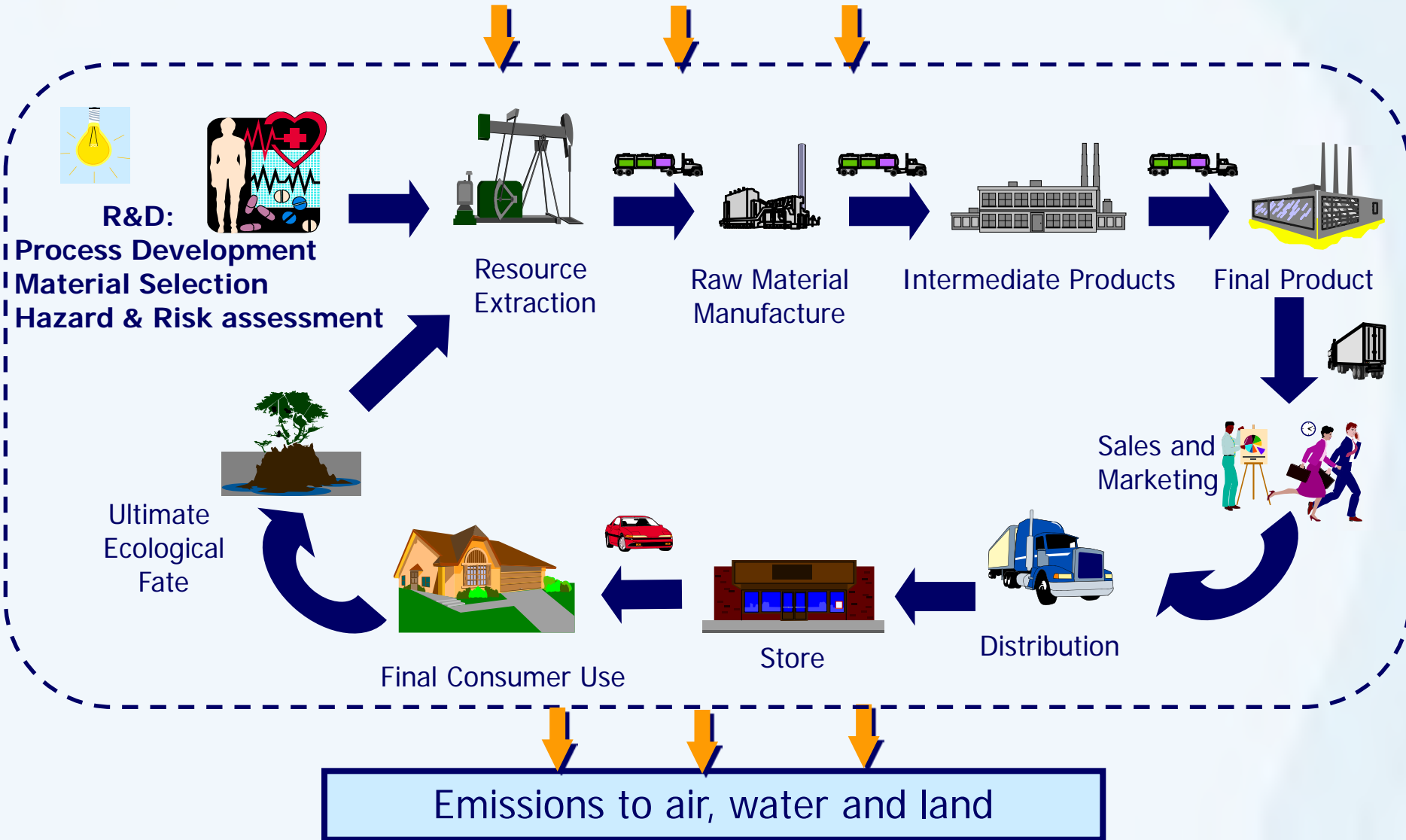




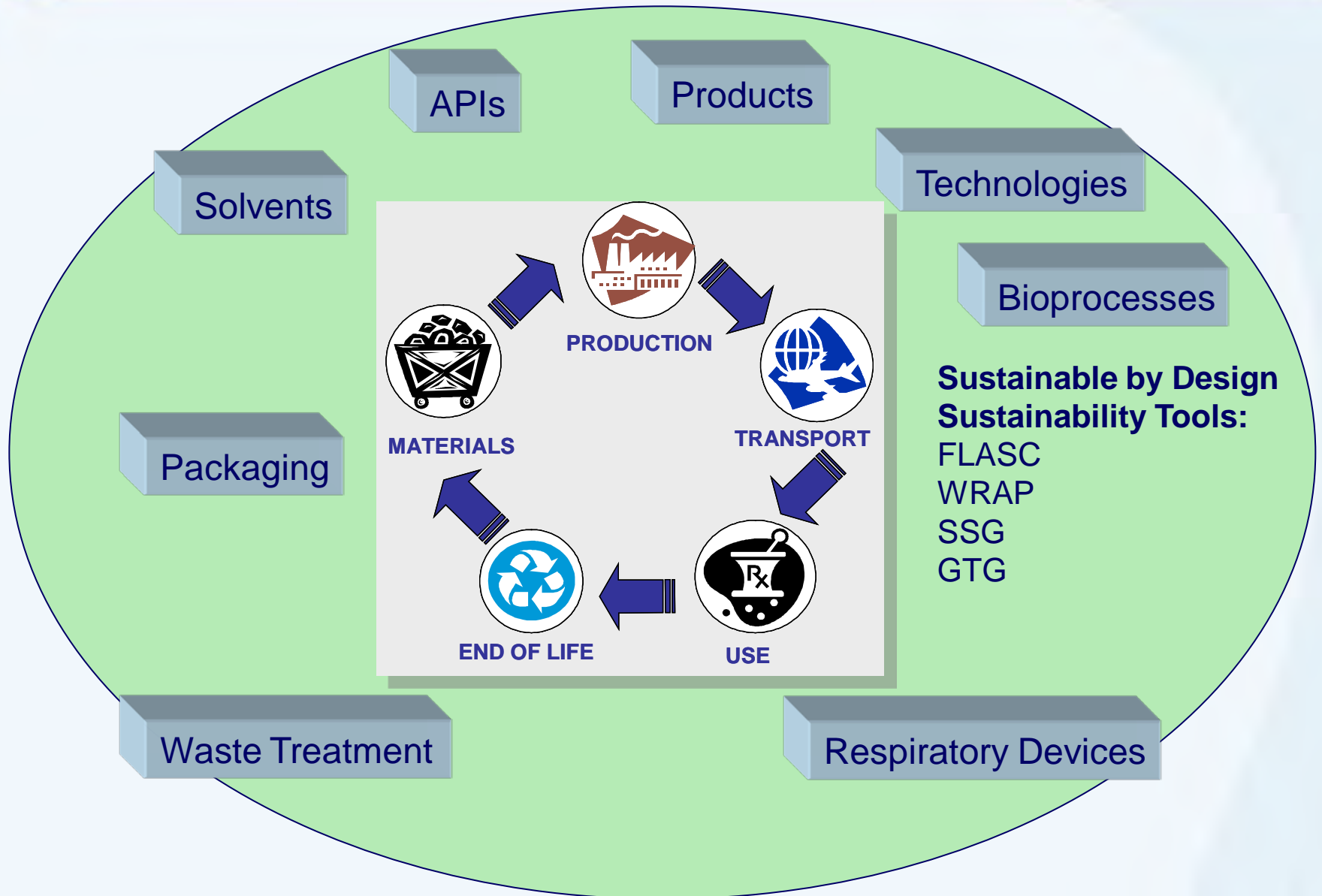
Sustainability – the bigger picture

Life Cycle Assessment

Raw material and energy consumption



LCI/A Program in GSK



Streamlined LCIA in GSK: FLASC™

Life cycle assessment score is a key operational metric for API development

The screenshot shows the FLASC web application interface. At the top left is the GSK logo. The main title is "Fast Lifecycle Assessment for Synthetic Chemistry (FLASC)". On the right, it says "© Copyright 2003 GlaxoSmithKline". A left-hand navigation menu includes: "Enter FLASC", "Getting Started", "Background", "Guidance for Route Improvement", "Quick Reference Guide", and "Help". Below the menu is the "Eco-design Toolkit" logo with "myEHS Community". The main content area features a banner image of a green frog with glasses and the text "Some are Born Green...". Below this, a paragraph explains that FLASC uses a "life cycle" approach to evaluate environmental consequences. A section titled "FLASC will:" lists two bullet points: "Compare or benchmark processes/routes and identify the greenest option" and "Provide guidance and identify the materials that have the biggest impact". Further down, it states: "For information on how the site was developed, and should be used and all the benefits it will deliver, see the **Background section**." Below that, it says: "Your assessments will be tracked via your LAN ID:". At the bottom of the main content area are two buttons: "Enter FLASC" and "Administration Module". A final banner at the bottom of the content area says "...Others make it happen!" with a small computer icon. The browser status bar at the very bottom shows "Done" and "Local intranet".

gsk
Fast Lifecycle Assessment for Synthetic Chemistry (FLASC)
© Copyright 2003 GlaxoSmithKline

Enter FLASC
Getting Started
Background
Guidance for Route Improvement
Quick Reference Guide
Help

Eco-design Toolkit
myEHS Community

Some are Born Green...

FLASC uses a "life cycle" approach to evaluate the environmental consequences of new or existing processes based around the input materials used. It quantifies the energy and materials used in their manufacture, as well as emissions released, and potential environmental impacts.

FLASC will:

- Compare or benchmark processes/routes and identify the greenest option
- Provide guidance and identify the materials that have the biggest impact

For information on how the site was developed, and should be used and all the benefits it will deliver, see the **Background section**.

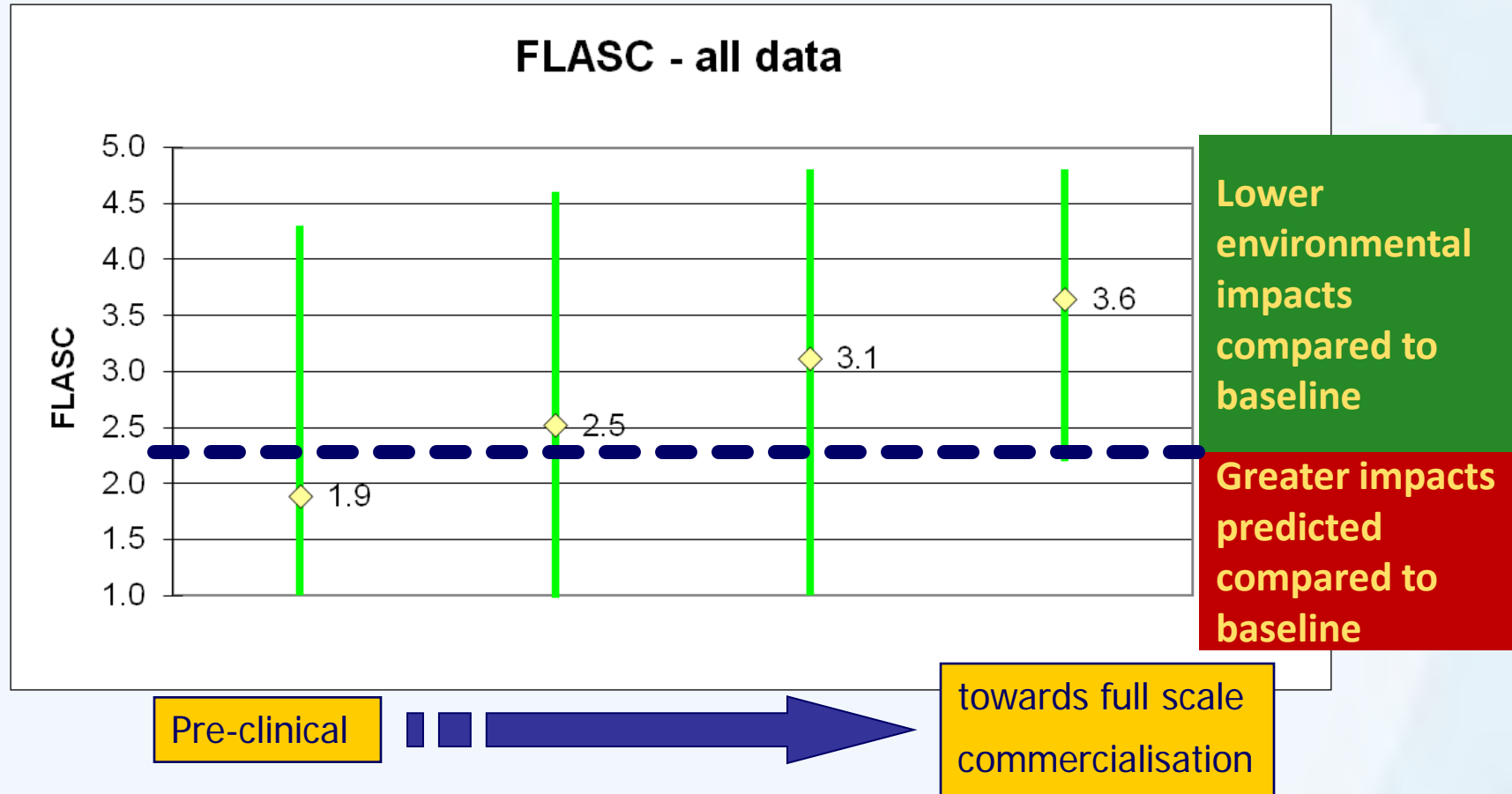
Your assessments will be tracked via your LAN ID:

Enter FLASC Administration Module

...Others make it happen!

Done Local intranet

Life Cycle Impact - FLASC scores



* 25 GSK routes developed during 1990 to 2000 were assessed.
The average performance was assigned a FLASC rating of 2.3

Summary

The strategy is to influence the development of next generation of drugs in development so they are greener

Green Metrics data reports help Project Teams understand their processes, highlight opportunities and monitor improvements

Analysis of the portfolio helps demonstrate improvements during development and highlights where further strategic opportunities lie

Summary

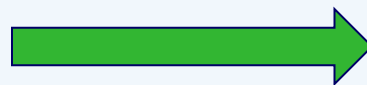
Solvents have the biggest environmental impacts of a process to manufacture an API

Finding a **green replacement** for **dichloromethane** remains a big challenge, though alternatives such as 2-MeTHF are starting to come through

GSK's life cycle assessment metrics continue to suggest that processes in development are **potentially greener** than the previous generation of API's

Ongoing Work and future Challenges

We have held
'Sustainability Day'
seminars to engage our
scientists



External insight from
world leading experts

Case studies

Debate and feedback

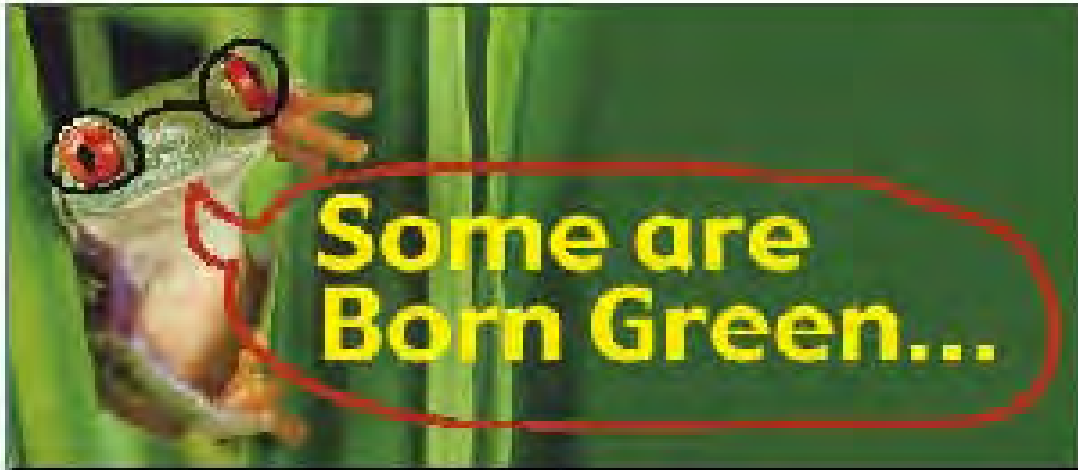
We are performing Life
Cycle Analyses of typical
products



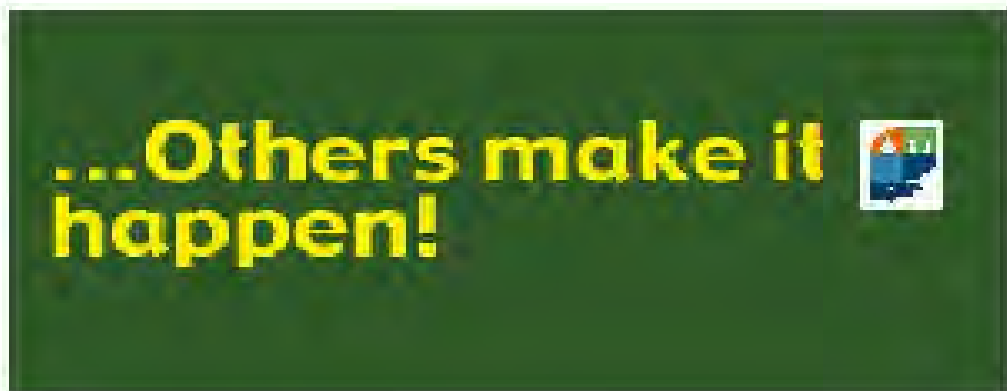
Using more renewable resources and cleaner technology

Acknowledgements

- GSK's Sustainable Processing Team
- Tom Roper
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- Julie Manley (ACS GCIPR)
- Ingrid Merglesberg (S-P)
- And many others....



Any Questions?



The Green Chemistry Website links to the other Design Tools

Green Chemistry Guide - Microsoft Internet Explorer

Address: <http://greenchemistry.gsk.com/>

Green Chemistry Guide

Core Principles

Chemistry Design

- Reactions
- Route Design
- Solvent Selection
- Base Selection
- Legislation Guide

Green Technology Guide

Process Design

- Chemistry Route
- Work up and Separations
- Solvents
- Green Champions
- Outsourcing

Some are Born Green...

- This site seeks to:
 - Reduce environmental, health and safety impacts;
 - Promote more efficient use of resources, including energy;
 - Minimise costs.
- The GSK Green Chemistry Website is designed to help scientists and engineers to better understand and apply Green Chemistry concepts to their work.

Please navigate through the website using the links on the left which take you through a series of guidance and advice.

Base Selection Guide - Microsoft Internet Explorer

Address: <http://baseguide.gsk.com/>

Base Selection Guide

New Interactive Base Select Guide and Information

Click on a base name for more information.

Base	Waste	Impact	Health	Safety	PK
Sodium hydride	10	7	1	1	35.0
Lithium diisopropylamide	3	2	1	1	40.0
Butyllithium	4	2	1	1	50.0
Lithium amide	6	1	1	1	35.0
Potassium hydroxide	10	7	4	7	15.7
Sodium hydroxide	10	6	4	7	15.7
Lithium hydroxide monohydrate	10	1	4	7	15.7

Solvent Selection Guide - Microsoft Internet Explorer

Address: <http://solventguide.gsk.com/>

Solvent Selection Guide

New Interactive Solvent Select Guide and Information

Click on a solvent name for portal to data on physical properties/EHS, Life Cycle and Separability.

SOLVENT	Waste	Impact	Health	Safety	Life Cycle	GMS use
Ethylene glycol	4	9	8	9	9	
1-Butanol	5	8	8	8	5	Ir
Diethylene glycol butyl ether	5	7	10	9	7	
2-Ethyl hexanol	9	6	8	7	6	U
Isoamyl alcohol	7	7	7	8	6	
2-Butanol	4	7	7	7	6	
Ethanol/EHS	6	6	10	7	9	C,D,Ir,T,U
2-Propanol	8	9	9	7	5	A,C,D,Ir,T,U,V
1-Propanol	4	7	5	8	7	D
t-Butanol	4	10	7	7	8	T
Methanol	4	10	5	8	9	A,C,D,Ir,T,U,V
Butyl acetate	7	8	9	8	5	
t-Butyl acetate	7	10	7	7	7	
Propyl acetate	6	7	8	7	5	
Isopropyl acetate	5	8	8	7	6	A,U,S
Ethyl acetate	4	8	8	4	6	A,C,D,Ir,T,U,V
Methyl acetate	7	10	7	5	7	W
Dimethyl carbonate	1	7	8	7	8	
p-Xylene	8	8	7	5	7	
Toluene	7	8	6	4	7	A,C,D,Ir,T,U,V
Fluorobenzene	4	7	4	5	7	A,C,D,Ir,T,U,V
Methylisobutyl ketone	7	6	6	7	7	A,Ir,S,T,W
Acetone	7	6	8	5	7	A,C,D,Ir,T,U,V

Life Cycle Assessment Tool - Microsoft Internet Explorer

Address: <http://greenchemistry.gsk.com/>

Fast Lifecycle Assessment for Synthetic Chemistry (FLASC)

Enter FLASC

Getting Started

Background

Guidance for Route Improvement

Quick Reference Guide

A new component of the Eco-Design Toolkit, FLASC is located at greenroute.gsk.com

FLASC uses a "life cycle" approach to evaluate the environmental consequences of new or existing processes based around the input materials used. It quantifies the energy and materials used in their manufacture, as well as emissions released, and potential environmental impacts.

Chemical Legislation Guide

HOME PAGE - UPDATED 19th MAY 2006

This web site was created to deliver the Chemical Legislation Guide, it is designed to help scientists and engineers identify those chemicals that are under legislative scrutiny. The guide is delivered through the EXCEL workbook [Chemical Legislation Guide v1.3a.xls](#) (updated 19th May 2006) which should be downloaded from below to ensure that you are referring to the latest version. Macros must be enabled for the workbook to function correctly.

The guide was compiled based on existing or imminent regulatory actions of different legislative bodies, but mostly those in the EU (See **Scope and Limitations**). These substances have been identified as having specific properties with known or suspected impacts to the environment or human health and therefore present unacceptable risks for continued GSK use.

This guide is not intended in any way to replace safety data sheets and is to be used in conjunction with Safety Data Sheets (SDS). **It does not incorporate comprehensive environmental, safety and health information or guidance and complements existing data in the SDS.** In some instances, data in an SDS may appear to be in conflict with the data or recommendations in the database. The user is therefore encouraged to seek guidance from EHS professionals when there is an apparent conflict in the recommendations in the Guide and in SDS.

This guide must be used in conjunction with the **Dangerous Chemical Pollutant Lists**.

You can download any of the files below by dragging them to your Windows desktop. To open a file for reading, double-click it.

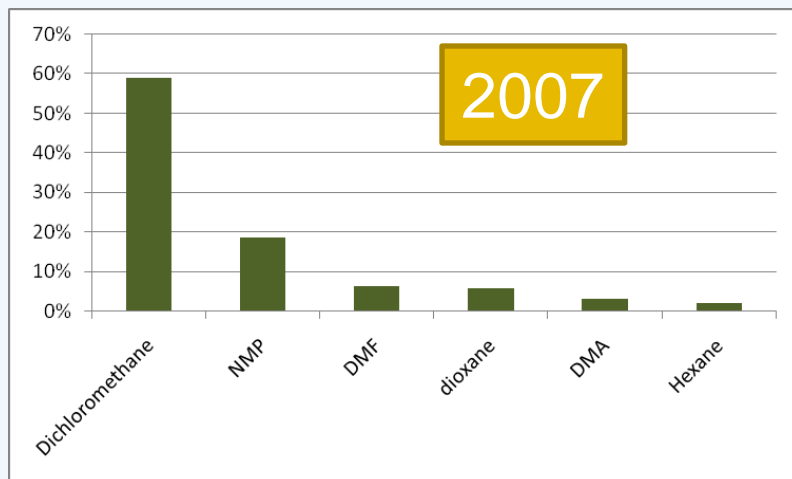
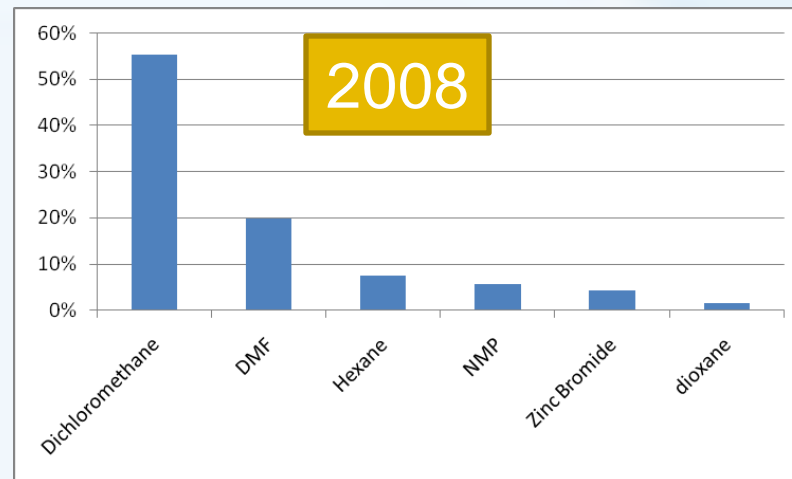
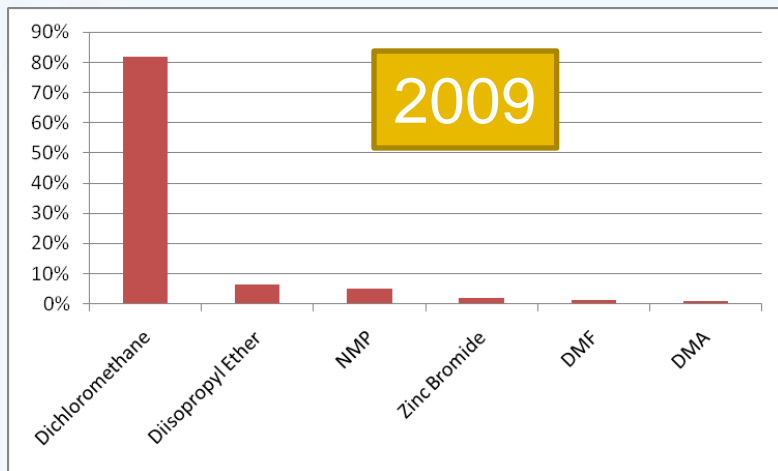
Processes/routes and identify the greenest option to identify the materials that have the biggest impact was developed, and should be used and all the benefits it will deliver, see the

via your LAN ID: constd00

Enter FLASC Administration Module

...Others make it happen!

Analyse the data - Materials of Concern



DCM and dipolar aprotics
are a common theme