GSK and Hazardous Chemicals Management

The Issue

Chemicals are used at every stage in pharmaceutical production. They are necessary to enable GlaxoSmithKline (GSK) to carry out fundamental research into the causes of disease, in the discovery of new medicines, in the manufacture of active pharmaceutical ingredients (API's) and in the formulation of our products. The types of chemicals used include reagents, catalysts, solvents, acids and bases, intermediates, surfactants, colours and flavourings and wide variety of excipients.

Many legal requirements have been introduced into international legislation over the years to protect people and the environment from the potential adverse effects of exposure to hazardous chemicals. However, while significant reductions in pollution from major industrial sources have been made, basic information on the public health and environmental hazards of many chemicals placed on the market for use in manufacturing processes and in everyday products is still lacking [1]. Moreover, advances in analytical technology have shown that many of these chemicals are widespread in the environment and can also be found in human tissues [2]. These factors have contributed to heightened societal concern about chemicals and doubts about the effectiveness of the regulatory systems to anticipate and prevent unacceptable human health and environmental impacts [3]. This has in turn led to developments in governmental chemicals policy such as the EU Registration, Evaluation and Authorisation of Chemicals Regulation (REACH) [4].

GSK recognises that hazardous chemicals must be used in a way that minimises any potential adverse effects on human health and the environment. Their use must therefore be based upon an understanding of the risk they present.

Any hazardous chemical used in our research activities is handled in small quantities by trained scientists under strictly controlled conditions that minimise any environmental emissions or workplace exposure and therefore does not represent a significant risk. The research phase of our product lifecycle is therefore not included in the scope of this position statement. The issue of pharmaceuticals in the environment is also precluded from this paper and is the subject of a separate public position statement. This statement instead focuses on GSK's use of larger quantities of chemicals such as during clinical development, in manufacturing operations and in our marketed products.

GSK's Public Position

- GSK supports the 2002 Johannesburg World Summit target to "*use and produce chemicals in ways which will lead to the minimisation of significant adverse effects on human health and the environment by 2020*".

- Careful management of the following classes of "priority chemicals" is central to GSK reaching our sustainability goals:

  - carcinogens, mutagens or reproductive hazards (CMR's),

- those known to be toxic and bioaccumulate or persist in the environment (PBT's)
- those known to very persistent or very bioaccumulative in the environment (vPvB)
- ozone depleting chemicals,
- endocrine disruptors
- those known to cause asthma

Criteria for assignment of substances to these classes are available in Appendix 1

- GSK has identified five priority activities that we believe help to ensure that the chemicals and products we produce or use do not adversely affect human health or the environment:

1) Hazard Assessment and Communication

A comprehensive understanding of intrinsic hazard is critical for decision making and the sound management of chemicals. We therefore:

- Use assessment approaches that identify the key environmental and workplace health and safety (EHS) hazards associated with GSK proprietary chemicals and products
- Implement robust processes to obtain EHS information on non-proprietary chemicals from our suppliers and published literature
- Provide relevant stakeholders (e.g. employees, contract manufacturers/key suppliers, customers, regulators etc) with chemical hazard information to enable them to adopt appropriate risk management approaches

2) Substitution of "Priority Chemicals"

We have adopted a chemicals management approach that applies, wherever possible, the substitution principle as the initial alternative. To that end, we:

- Identify "priority chemicals " that we currently use, using the criteria in Appendix 1
- Actively assess the feasibility of using alternative, less hazardous chemicals
- Focus on the development phase of new products to identify when and where these less hazardous chemicals may be used
- Replace "priority chemicals" in our existing products and manufacturing processes, if this is technically and economically feasible
- Adopt appropriate and responsible risk management approaches where elimination or substitution is not possible

Key performance metrics relating to substitution of hazardous chemicals are reported in the GSK Corporate Responsibility Report.

3) Transparency

We are committed to openness and transparency about how we manage hazardous chemicals and will continue to engage with relevant stakeholders and make the following information publicly available:

- What we consider to be a "priority chemical"
- Progress on initiatives designed to eliminate or substitute "priority chemicals"
- Information on risk management strategies developed to support continued use of any "priority chemical"
- Environment, health & safety data on our products using safety data sheets published on gsk.com

4) Supply Chain Management

We believe that we should play a role in encouraging responsible management of hazardous chemicals throughout our supply chain and apply consistent standards to our contract manufacturing operations. This is achieved by**:**

- Requiring that our suppliers comply with all legal and regulatory requirements
- Establishing global EHS requirements for key suppliers and contract manufacturers and where appropriate conducting pre-contract EHS evaluations of potential suppliers
- Conducting periodic audits against these requirements and where necessary providing encouragement and assistance to help contract manufacturers and key suppliers to improve their EHS performance
- Including robust EHS management systems and "responsible care" programmes in the criteria for the selection of key suppliers and contract manufacturers of priority chemicals

Selected EHS performance metrics for key suppliers and contract manufacturers are reported in the GSK Corporate Responsibility Report

5) Sustainable Chemistry

We believe that the principles of “green chemistry” play an important role in the management of hazardous chemicals [5]. Therefore we will continue efforts to identify opportunities to adopt sustainable chemical technologies including:

- Improving process design and efficiency to minimise the use of chemicals and reduce associated waste or emissions
- Identifying opportunities to use less hazardous chemicals and ensuring any residual risks are appropriately managed
- Exploring opportunities for the use of renewable resources and biotransformations
- Using inherently safer chemistry
- Minimising energy- and water-intensive manufacturing processes
- Exploring and optimising recycling and reuse opportunities

Key performance metrics relating to sustainable chemistry have been developed and are reported in the GSK Corporate Responsibility Report.

BACKGROUND

<u>GSK and the Legislative Environment</u>

The manufacture, transport and supply of chemicals and their use in our operations are governed by a substantial body of legislation enacted to protect health & safety and the environment. For example over the last 40 years, the EU has generated more than 500 Directives and associated instruments relating to chemicals and consumer protection, occupational health, environmental protection, process and transport safety and hazardous substance management. Through our Global EHS Standards, we comply with all regulatory requirements. Moreover, where a GSK operation is subject to both GSK and regulatory requirements, the stricter requirement will apply.

GSK and “Green Chemistry”

In addition to regulatory compliance, GSK is committed to the principle of product stewardship and has an active “green chemistry” programme aimed at developing more sustainable manufacturing processes. For example in 2010 we announced an important partnership with the Singapore Economic Development Board, committing S$50 million (£24 million) in funding to support research in green and sustainable manufacturing.

Since 2005 we have achieved significant results in minimising the use of hazardous chemicals as we have developed new pharmaceutical products. On average our R&D processes substituted or eliminated 95% by mass of substances identified as “priority chemicals” (when normalised per kg drug substance produced). In 2010 seven solvents accounted for about 80% of the priority chemicals used. Most of the solvent waste was destroyed by incineration, although some was recycled.

Chemical Substitution

In addition to green chemistry initiatives we have been successful in substituting hazardous chemicals in our product portfolio. This is exemplified by our success in phasing out use of CFC’s as a propellant from our metered dose inhalers for asthma and replacing triclosan in many of our oral healthcare products.

The pharmaceuticals sector is unique in that, quite rightly, there are very strict regulatory and quality requirements imposed to ensure that any changes in manufacturing do not adversely affect the safety or efficacy of the medicine. This means that before considering the substitution of an existing process chemical we must ensure that any replacement fits with the chemistry of the manufacturing process and validate that the change has not affected the efficacy or patient safety profile of the medicine. Consequently, it is not always technically feasible to substitute chemicals in many existing manufacturing processes and even if it is possible the cost of making such changes may be prohibitive. As a result substitution or elimination of hazardous chemicals from GSK synthetic routes, formulations and products tends to be focused on new product development activities.

Further Background Information

1. Allanou R., Hansen BG., and van der Bilt Y (1999). Public availability of data on EU high production volume chemicals. EU 18996 EN European Chemicals Bureau, Ispra, Italy
2. Thornton JW., McCally M., and Houlihan J (2002). Biomonitoring of Industrial Pollutants: Health and Policy Implications of the Chemical Body Burden. Public Health Reports 117, 315-323
3. Royal Commission on Environmental Pollution. Twenty-fourth Report. Chemicals in Products; Safeguarding the Environment and Human Health. June 2003
4. European Commission (2001) Strategy for a future chemicals policy. COM (2001)88. Brussels: European Commission
5. Green Chemistry: Theory and Practice. Paul Anastas and John Warner. Oxford University Press. 1998

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