GSK Public policy positions

Genetically Modified Micro-organisms and Environment, Health & Safety

The Issue

GSK is in the forefront of the development and application of new scientific techniques to discover and develop new medicines and vaccines. This includes the safe and responsible use of genetically modified micro-organisms (GMM), by which we mean microbiological entities such as bacteria, fungi, viruses, viroids, animal or plant cells in culture, which are developed and used in contained environments.

There are a number of benefits associated with the use of GMM in the research, development and manufacture of medicines. For example, the use of GMM technology has enabled GSK to:-

- develop a Hepatitis B vaccine without using human blood products, eliminating the inherent risk of infection from contaminated source material.
- reduce the pathogenicity of micro-organisms used when developing and producing vaccines or when developing new GMM vectors, making them safer to handle, and allowing us to use containment controls with a reduced energy requirement.
- reduce the use of animals when producing monoclonal antibodies.
- construct micro-organisms that have a reduced capacity to survive outside of the manufacturing process compared to naturally produced micro-organisms.
- produce therapeutic proteins that could not be made using conventional chemistry.
- reduce the environmental impact of manufacturing some of our active pharmaceutical ingredients by using specially developed biocatalysts that result in higher yields from our manufacturing processes.

Notwithstanding these benefits, however, GSK recognises that the use of GMM technology may cause concern. This paper sets out what we believe to be an effective and responsible approach to assess and manage potential risks associated with the use of GMM.

GSK's Position

- **All work with GMM within GSK is assessed and controlled applying the best practice across all our facilities.**

  - We adopt a responsible approach to the use of GMM. We follow our global Sustainability, Environment, Health and Safety standards to ensure any risks of handling GMM are minimised. Our standards meet or exceed the requirements of local, national and international regulations.

- **GSK is committed to ensuring that we control the risks to our employees and the environment when we use GMM technology to develop and manufacture products.**

  - GSK has procedures that ensure the hazards and risks associated with the development and manufacture of its new products are thoroughly assessed and controlled.

    - Any work with GMM is subject to a risk assessment to identify appropriate controls including safe conditions of use, storage, disposal and emergency management procedures to minimise contact between GMM, humans and the environment.
    - We manage the use of GMM through bodies such as site Institutional Biosafety Committees (IBC) or Genetic Modification Safety Committees (GMSC) in line with national and local regulations.

- **GSK is committed to the control of environmental, health and safety risks throughout our manufacturing supply chains, including third-party manufacturers.**

  - This principle is central to product stewardship, which means taking responsibility for a product throughout its whole life cycle, i.e. during its development, manufacture, use and disposal. We expect our business partners to meet similar standards for EHS and quality to those required from our own factories and we audit contract manufacturers to ensure appropriate standards are maintained.

  - We communicate information and guidance for employees, customers, contract manufacturing partners and onward users on the safe processing, usage, transportation and disposal of any GMM or products derived from GMM.

- **GSK requires that GMM are inactive in waste streams to ensure safety to human health and the environment.**
  - We evaluate the risks associated with the GMM that we use and employ processes that are effective in inactivating waste streams to ensure protection to human health, safety and the environment.

- **GSK is committed to openness and transparency about how we manage risks associated with use of GMM and continue to engage with stakeholders to enable us to understand and keep in touch with their views.**
  - Much of our engagement takes place through day-to-day interactions with customers, employees, suppliers and other partners, but we are also involved in more structured engagement through meetings and participation in conferences.

Background

What are the differences between using regular micro-organisms and Genetically Modified Micro-organisms (GMM)?

There are differences in the levels of deactivation required for GMM compared to regular micro-organisms before waste streams that potentially contain GMM are released into the environment. The regulatory framework governing the release and treatment of GMM differs widely in different geographic areas. As a globally responsible company, GSK is applying the best, most responsible practices globally, independently of regulatory differences. This position statement is supported with detailed technical guidance for those teams that use GMM in their work.

What are the differences between Genetically Modified Organisms (GMO) and Genetically Modified Micro-organisms (GMM)?

GMOs are organisms that have had their DNA altered by gene technology. This grouping includes transgenic animals and GM crops which can interact with the environment. GMM are a sub-set of GMO. They are microbiological entities (such as bacteria, fungi, viruses, viroids) or animal/plant cells in culture, which are developed and used in contained environments, such as in reaction or fermentation vessels.

What is Gene technology?

Gene technology encompasses a range of techniques whereby nucleic acids are manipulated to modify protein production or to make new proteins. Genetic modification technologies can alter the genetic make-up of an organism to introduce traits that cannot be acquired through the process of traditional reproduction.

What is a Risk Assessment for GMM?

Risk assessment involves the classification of the GMM work into one of four categories (Risk Groups 1-4 with increasing containment requirements) based on the hazards present associated with the host, donor DNA or the product. These categories are described in the Scientific Advisory Committee on Genetic Modification Compendium of Guidance[1] in the UK and the NIH Guidelines for Working Safely with rDNA[2] and in the brochure Biosafety in Microbiological and Biomedical Laboratories[3] the US. Other countries have similar guidelines. The classification outcome determines the containment measures required to control the identified risks.

What measures are in place to contain GMM?

GMM are contained using measures to limit contact between GMM, humans and the environment. These can be:-
- Physical: such as engineered containment, sealed fermenters, the use of biosafety cabinets, the physical containment of laboratory ventilation systems

– Chemical: such as using disinfectants, or changing the pH of a process stream
– Thermal: such as heat sterilisation processes
– Biological: such as the use of disabled strains, for example, whose growth and survival depends on the addition of nutrients not available in humans or in the environment outside of culture media

How are GMM inactivated in a waste stream?

The strategies used for inactivating a GMM-containing waste stream are determined by the nature of the GMM being used, the concentration of the material in the waste stream, the volume of the waste stream, the ability of the GMM to survive in a natural environment, and the viability of the cells after processing.
Methods to inactivate waste streams can include:-

– Heat treatment
– Chemical treatment
– Physical disruption of cells
– Filtration
– Radiation (gamma or UV)

The Regulatory Framework

Europe

The European Union (EU) makes a distinction between GMOs and GMMs; specifically GMM are defined, controlled and regulated through EU Council Directive 2009/41/EC on the contained use of genetically modified micro-organisms[4]. GMO on the other hand are controlled through EU Council Directive 2001/18/EC on the deliberate release into the environment of genetically modified organisms[5], such as from the deliberate planting and cultivation of GM crops.

The US

In the US there are no specific regulations for genetically modified organisms or micro-organisms. The three agencies involved (US Department of Agriculture, the US Food and Drug Administration and the US Environmental Protection Agency) all use existing regulations for their governance processes:

– Plant Protection Act (PPA);
– Federal Insecticide, Fungicide and Rodenticide Act (FIFRA);
– Federal Food, Drug, and Cosmetic Act (FFDCA);
– Toxic Substances Control Act (TSCA).

Under this framework, the FDA is responsible for biotechnologically-derived medical products; the USDA for transgenic plants and the EPA for pesticidal plants and genetically-engineered microbial pesticides. However, most institutions, including GSK, voluntarily adhere to the National Institutes of Health (NIH) Guidelines for Research Involving Recombinant DNA Molecules[2]. The NIH Guidelines define recombinant DNA molecules as either:

> *…(i) molecules that are constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell, or (ii) molecules that result from the replication of those described in (i) above.*

These guidelines are only mandatory for those institutions receiving Federal grant funding for rDNA research.

Other countries also regulate work with GMM through specific legislation.

The GSK Standards

GSK has developed Global Sustainability, Environment, Health and Safety standards which are used to set the governance of all environment, health and safety issues in the company. These standards set out the requirements expected of teams, which can be met by following the approaches laid out in accompanying technical guidance documents. As our standards meet or exceed the requirements of local, national and international regulations, we ensure regulatory compliance.

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[1] The Scientific Advisory Committee on Genetic Modification Compendium of guidance, Health and Safety Executive, Hazardous Installations Directorate, Specialised Industries Division, Biological Agents Unit, 1.2 Redgrave Court, Merton Road, Bootle, Merseyside L20 7HS, http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/ last accessed 12th November 2009.

[2] The NIH Guidelines for Research Involving Recombinant DNA Molecules, amended September 2009, US Department Of Health And Human Services, National Institutes of Health, Office of Biotechnology Activities, Office of Science Policy - National Institutes of Health, USA, http://oba.od.nih.gov/oba/rac/guidelines_02/NIH_Guidelines_Apr_02.htm, last accessed 12th November 2009.

[3] Biosafety in Microbiological and Biomedical Laboratories (BMBL), U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, and National Institutes of Health Fifth Edition, Feb 2007, http://www.cdc.gov/od/ohs/biosfty/bmbl5/bmbl5toc.htm, last accessed 13th November 2009.

[4] EU Council Directive 2009/41/EC on the contained use of genetically modified micro-organisms, http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:125:0075:01:EN:HTML last accessed 13th November 2009.

[5] EU Council Directive 2001/18/EC on the deliberate release into the environment of genetically modified organisms, http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2001:106:0001:0038:EN:PDF, last accessed 6th July 2009.