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Society for General Microbiology Statement on Genetic Modification

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Summary

The Society for General Microbiology is supportive of the use of genetic modification (GM) technology in research, subject to appropriate regulation and ethical review. Its medical, industrial and agricultural use is also supported if scientific, economic and ethical review indicates that GM technology offers distinct advantages over other methods and is safe.

Uses of GM in microbiology

Research tool: Research microbiologists routinely use genetically-modified (or 'engineered') microorganisms, laboratory animals (primarily, mice) and genetically-modified plants in laboratory studies of infectious disease, microbial physiology and other processes.¹ Examples of laboratory research where microbiologists use GM include protein localisation with Green Fluorescent Protein; and gene expression experiments with beta-galactosidase or luciferase. Such experiments were not possible before the advent of GM in the 1970s and have, without doubt, spurred scientific discovery, contributing to innovation in medicine, industry and agriculture.

Manufacturing process: Since the 1980s, manufacturing firms have employed GM bacteria and fungi in a small number of industrial applications, mainly in the chemical, pharmaceutical and food industries. Recombinant insulin was the first such product, marketed since 1982 by the American pharmaceutical company Eli Lilly. Other such products have included vegetarian rennet, growth hormone, interferon and 1,3-propanediol, a chemical used in the manufacture of polyester fibre.²

Vaccines: GM technology is used to make vaccines against infections such as human papilloma virus and hepatitis B. The 'FLUENZ' influenza vaccine is one very recent development that could be vital in a flu pandemic.³ Veterinary vaccines include the oral rabies vaccine V-RG (Case study 1, below) and vaccines against Newcastle and Marek's diseases in poultry.⁴

Disease resistance 'by design' in crops and livestock: GM technology can, in principle, be used to protect crops and livestock from disease (Case study 2). To our knowledge, authorities around the world have approved 15 disease-resistant GM crop varieties for commercial growing (seven in potato; three in papaya; two in squash; and one each in bean, plum and sweet pepper). A further ten disease-resistant crop varieties are in advanced development for commercial use. In 2011, UK scientists used GM technology to develop a chicken unable to transmit bird flu, but commercialisation of the technology is many years away.⁵ Crops genetically modified for disease

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romoting modern microbial science

resistance are not grown in the EU.⁶ There are currently no commercially-available GM livestock with disease-resistance traits.

Environmental release

As a research tool or a manufacturing process, GM is considered to be 'contained' within a laboratory or industrial premises, and there are mandatory precautions to ensure containment. European regulatory authorities only permit environmental releases after a lengthy review, if at all. In the case of manufactured goods, GM material is removed during the production process – hence, the material should not be present in the finished product and does not appear in the food chain or the environment.⁷

Assessing the worth of GM

Over the past 30 years, genetic modification technology has yielded products and processes that are genuinely useful. The technology may continue to do so in the future. However, as with all technologies, we do need good, proportionate regulation, and publically-accountable legislative, economic and ethical review.

Claims for the worth of each new GM product need to be backed by evidence for economic, social and/or health benefits, benchmarked against existing or next-best solutions.⁸ Regulators should also take into account scientific assessments of the safety of particular GM technologies for both people and the environment. No technology should be intentionally developed to have detrimental effects.

SGM believes in upholding appropriate standards of physical and biological containment for research on GM and non-GM micro-organisms, subject to suitable regulation and ethical review. This criterion should also apply to the use of emerging biotechnologies such as synthetic biology.

Our two case studies (below) are intended to highlight the varied uses of GM technology, but also the difficulties of conducting technology assessments that take into account longer-term economic and other factors.

We are not aware of any peer-reviewed epidemiological studies showing detrimental health effects attributable to GM crops in countries where such crops are consumed on a large scale, e.g., the USA. However as the World Health Organization has indicated, there is also the need for continual follow-up to ensure that we identify emerging health risks.⁹ Monitoring over the long term is essential.

SGM will in all cases strive to inform debates about the development and use of GM technologies as they impact microbiology, according to the highest standards of independent scientific evidence.

Case study 1 – Rabies and red foxes

Rabies is an infectious disease of wildlife, domestic animals and people. Without treatment, the disease is fatal. Rabies circulates in an animal reservoir – primarily red foxes. Accordingly, the risk of an outbreak can be reduced either by culling foxes or by vaccinating them.

The story begins in the 1960s when the American microbiologist George Baer and his colleagues developed 'attenuated' viral vaccines that could be hidden in bait for the fox to (unwittingly) swallow. They made these vaccines by repeatedly infecting and re-infecting cells with the rabies virus; in the course of this 'serial passage', mutations in the viral genome arose naturally that rendered the virus infective but unable to cause disease.¹⁰ The first field trial occurred in Switzerland in 1978 and proved the method effective at controlling rabies.¹¹

Six years later, another team of scientists – working variously at the non-profit Wistar Institute, the US government's National Institute of Allergy and Infectious Disease and the Strasbourg-based biotech firm Transgène – developed the V-RG recombinant rabies vaccine.¹² Instead of relying on natural mutations as Baer had done, they used genetic engineering methods to insert a glycoprotein-coding gene from rabies into the cowpox (vaccinia) virus. The French vaccine maker Mérial commercialized the product under the 'Raboral' trade-name.

The Belgium government was the first in the world to use recombinant vaccine. Between 1989 and 2000, they distributed (mostly by helicopter) three million vaccine doses over 10,000 square kilometres of their own territory and adjoining countries; 92 % of the doses were GM.¹³ Although this Belgium programme is little-known, it was (and is) the largest dissemination of a genetically-modified organism anywhere in Europe.¹⁴

How useful has the approach been? To evaluate the effectiveness and safety of the recombinant vaccine, Belgium scientists conducted a series of trials.¹⁵ These data convinced them that the V-RG vaccine was more effective than existing, non-GM, vaccines. In particular, that V-RG was more heat stable and would last longer in the bait. They also considered it less likely to transform into a dangerous, rabies-causing type, unlike attenuated vaccine which does sometimes transform, albeit at a low rate.¹⁶

Rabies in people, domestic animals and wildlife in Belgium declined during the GM vaccination campaign. In 2001, both the World Health Organization and the World Organisation for Animal Health declared Belgium 'free of rabies'.¹⁷

Belgium, France and Luxembourg have been the only European countries to adopt the recombinant vaccine – American and Canadian authorities have also used recombinant vaccines on a large scale.¹⁸ Nevertheless, non-recombinant vaccine has been seen as sufficient elsewhere. Italy organized a campaign using only an attenuated vaccine and was certified 'rabies-free' in 1997.¹⁹ Disease rates have fallen under both the attenuated and GM control regimes.²⁰

Rises in the number of foxes, associated with reductions in disease, have led some to argue that rabies eradication, by whatever method, might disrupt the ecological balance.²¹ Against that, we have to weigh the gains that control brings in terms of animal welfare and our own safety. Rabies remains a devastating disease and, even in 'rabies-free' countries, sporadic cases still occur.²²

Point and counterpoint

Brochier, B., Costy, F., Peharpre, D., Mosselmans, F., Beier, R., Escutenaire, S., Dechamps, P., Leuris, J., Villers, M., Lecomte, L., Mullier, P., Roland, H., Bauduin, B., Kervyn, T., Renders, C. & Pastoret, P. P. (2001). Elimination de la rage en Belgique par la vaccination du renard roux (*Vulpes vulpes*). Ann *Med Vet* 145, 293-305.

McNally, R. (1995). Mad dogs or jackasses? The European rabies eradication programme, in: *Animal Genetic Engineering: of Pigs, Oncomice and Men* (ed. Wheale, P. & McNally, R.), Pluto Press, pp. 109-123.

Case study 2 – Hawaiian papayas

Papaya ringspot virus (PSV) is the major infectious disease threat to papayas worldwide, causing chlorosis, stunting and spots on the fruit.²³

The virus became a problem in the Hawaiian papaya industry in the 1950s, leading to a crisis in production.²⁴ The industry relocated from the virus-infested Oahu Island to the virus-free 'Big Island' (Hawaii). But the virus had not gone away and, by late 1994, the re-located papaya industry succumbed to a second crisis due to the spread of the disease.

Hawaii Department of Agriculture officials had been working on disease control measures since the late 1970s. These included: conventional plant breeding to produce resistant varieties; 'cross-protection' (akin to vaccination); and the use of the glyphosate herbicide to rapidly kill infected trees, thus stopping spread.

In 1986, researchers at the University of Hawaii, Cornell University, and the Hawaiian agriculture department, led by Dr Dennis Gonsalves, began work on a GM papaya that would resist the virus. After 5 years of experiments, they succeeded in introducing a gene coding for the virus' 'coat' protein into the red-fleshed 'Sunset' papaya variety. Based on experiments with the related tobacco mosaic virus, they believed this would make the plant resistant – an assumption that turned out to hold true in greenhouse tests.

The researchers then used conventional crossing to breed the transgenic Sunset type with the yellow-fleshed 'Kapoho' papaya, which is grown commercially in Hawaii, producing a hybrid 'Rainbow' cultivar that proved resistant to the virus in field trials. Following a two-year long regulatory assessment that ended in 1998, the GM papaya was authorized for cultivation (and sale) in the USA.

Agricultural extension officers distributed the GM seeds free of charge.²⁵ The researchers handed over the patents to the Papaya Administrative Committee, an organization which represented papaya growers.²⁶

One problem was that transgenic papayas were not licensed for sale in Japan, a big market for Hawaiian growers (in 1992, about 35 % of Hawaii's papayas went to Japan – the remainder going to the American mainland).²⁷ Gonsalves and his colleagues designed a planting strategy, sowing 'breaks' of transgenic crop to halt the spread of the virus (GM fruits were then legally sold into the mainland market). These breaks were interspersed with stands of the non-transgenic variety intended for export to Japan.²⁸

The majority of papayas sown on the islands are now GM.²⁹ A 2006 study by the testing company Genetic ID, funded by the local campaign group Hawaii SEED, even picked-up the GM transgene in 50 % of 'non-GM' papaya seeds (from 60 papaya fruits sampled from backyards and organic farms across the Big Island).³⁰

As of December 2011, the Japanese government authorized the import of GM papayas from Hawaii, opening up a large market.³¹ Yet the Hawaiian papaya industry has, until now, been in long-term decline.

US Department of Agriculture figures indicate that harvested acreage, yield per acre and production have halved on the islands since a peak in the mid-1980s.³² This decline has occurred despite the introduction of GM in 1998 – and can be attributed to long-term falls in the market price, relative to inflation. Transgenic technology had short-term benefits in cutting rates of plant disease, but the *economic* fate of the industry has more complex determinants.

Point and counterpoint

Gonsalves, D. (2004). Transgenic papaya in Hawaii and beyond. AgBioForum 7, 36-40.

Greenpeace International (2006). The Failure of GE Papaya in Hawaii.

Notes and references

¹ For a review of early developments in genetic engineering and their implications, see: **Bull, A. T., Holt, G. & Lily, M. D. (1982).** *Biotechnology: International Trends and Perspectives,* Organisation for Economic Cooperation and Development, pp. 29-34.

² For a list of products, see: **Commission on Life Sciences (1992).** *Putting Biotechnology to Work: Bioprocess Engineering*, National Academies Press, p. 52. For information on 1,3-propanediol, see: **Genencor (2001).** Genencor International and DuPont Expand R&D Collaboration to Make Key Biobased Polymer, Press Release, 12 March 2001. http://bit.ly/VVTZm6_(Accessed 23 Jan 2013). With the exception of those products named in the text, the bulk of such products, while GMOs, are *not* produced in bacterial cells. For a discussion of why this is so, see: **Kamionka, M. (2011).** Engineering of therapeutic proteins production in *Escherichia coli. Curr Pharm Biotechnol* **12**, 268-274.

³ European Medicines Agency (2012). Product information. Fluenz. Annex I: Summary of product characteristics, p. 2, 27/11/2012. <u>http://bit.ly/VrsNuy</u> (Accessed 23 Jan 2013).

⁴ Meeusen, E. N. T., Walker, J., Peters, A., Pastoret, P. P. & Jungersen, G. (2007). Current status of veterinary vaccines. *Clin Microbiol Rev* 20, 489-510 (pp. 491 & 496).

⁵ Lyall, J., Irvine, R. M., Sherman, A., McKinley, T. J., Núñez, A., Purdie, A., Outtrim, L., Brown, I. H., Rolleston-Smith, G., Sang, H. & Tiley, L. (2011). Suppression of avian influenza transmission in genetically modified chickens. *Science* 331, 223-226. A listing of reports of GM livestock resistant to disease is given by: Van Eenennaam, A. L. & Muir, W. M. (2012). Animal biotechnologies and agricultural sustainability, in: *The Role of Biotechnology in a Sustainable Food Supply* (ed. Popp, J., Matlock, M. Kemper, N. & Jahn, M.), Cambridge University Press, p. 96.

⁶ Analysis based on data in: **Stein, A. J. & Rodríguez-Cerezo, E. (2009).** *The global pipeline of new GM crops: Implications of asynchronous approval for international trade,* European Commission/Joint Research Centre & Institute for Prospective Technological Studies; and **Anon. (2011).** *Approvals of GMOs in the European Union,* EuropaBio: the European Association of Bioindustries.

⁷ Anon. (1998). Council Directive 98/81/EC of 26 October 1998 amending Directive 90/219/EEC on the contained use of genetically modified micro-organisms, *Official Journal of the European Communities*; Anon. (2001). Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC, *Official Journal of the European Communities*. There have been recent changes to the regulatory posture: **European Commission (2010).** Communication from the Commission to the European Parliament, the Council, the Economic and Social Committee and the Committee of the Regions on the freedom for member states to decide on the cultivation of genetically modified crops, pp. 2-4.

⁸ For a detailed review of the socio-economic arguments around GM technology, see: **Spök, A. (2010).** *Assessing Socio-Economic Impacts of GMOs: Issues to Consider for Policy Development*, Bundesministerium für Gesundheit [Austrian Federal Ministry of Health]. For the UK context, see: **Cabinet Office Strategy Unit (2003).** *Field Work: weighing up the costs and benefits of GM crops,* July 2003, pp. 29-81.

⁹ World Health Organization (undated). '20 questions on genetically modified foods, Q8. Are GM foods safe?' <u>http://bit.ly/VVUT25</u> (Accessed 23 Jan 2013).

¹⁰ Baer, G. M., Abelseth, M. K. & Debbie, J. G. (1971). Oral vaccination of foxes against rabies. *Am J Epidemiol* 93, 487-490.

¹¹ Wandeler, A. I., Capt, S., Kappeler, A. & Hauser, R. (1988). Oral immunization of wildlife against rabies: concept and first field experiments. *Clin Infect Dis* **10**, S649-S653.

¹² Wiktor, T. J., Macfarlan, R. I., Reagan, K. J., Dietzschold, B., Curtis, P. J., Wunner, W. H., Kieny, M. P., Lathe, R., Lecocq, J. P. & Mackett, M. (1984). Protection from rabies by a vaccinia virus recombinant containing the rabies virus glycoprotein gene. *Proc Natl Acad Sci USA* **81**, 7194-7198.

¹³ Numbers calculated from Table 1 (p. 296) of: Brochier, B., Costy, F., Peharpre, D., Mosselmans, F., Beier, R., Escutenaire, S., Dechamps, P., Leuris, J., Villers, M., Lecomte, L., Mullier, P., Roland, H., Bauduin, B., Kervyn, T., Renders, C. & Pastoret, P. P. (2001). Elimination de la rage en Belgique par la vaccination du renard roux (*Vulpes vulpes*). Ann Med Vet 145, 293-305.

¹⁴ Note about programme being little-known from: Casse, F. & Breitler, J.-C. (2001). OGM:

description, méthodes d'obtention, domaines d'application, France Agricole Editions, p. 131.

¹⁵ Pastoret, P. P., Brochier, B., Languet, B., Thomas, I., Paquot, A., Bauduin, B., Kieny, M. P., Lecocq, J. P., De Bruyn, J., Costy, F., *et al.* (1988). First field trial of fox vaccination against rabies using a vaccinia-rabies recombinant virus. *Vet Rec* 123, 481-483. Brochier, B., Kieny, M. P., Costy, F., Coppens, P., Bauduin, B.,

Lecocq, J. P., Languet, B., Chappuis, G., Desmettre, P., Afiademanyo, K., *et al.* (1991). Large-scale eradication of rabies using recombinant vaccinia-rabies vaccine. *Nature* **354**, 520-522.

¹⁶ For vaccine properties, see: Brochier, B., Coppens, P. & Pastoret, P. P. Undated typescript, Oral vaccination of foxes using a vaccinia-rabies recombinant virus: programme of sylvatic rabies control in Belgium, pp. 159-162. http://bit.ly/ViM98D (Accessed 23 January 2013). The low risk of transformation in the non-transgenic vaccine is indicated in, e.g., Fehlner-Gardiner, C., Nadin-Davis, S., Armstrong, J., Muldoon, F., Bachmann, P. & Wandeler, A. (2008). ERA vaccine-derived cases of rabies in wildlife and domestic animals in Ontario, Canada, 1989-2004. J Wildl Dis 44, 71-85.

¹⁷ Brochier, *et al.* (2001). *Ibid.*, p. 303.

¹⁸ **US Department of Agriculture (2012).** News Release, 14 February 2012, USDA Distributes Oral Rabies Vaccine in Florida. <u>http://1.usa.gov/UkRNEH</u> (Accessed 23 January 2013). **Ministry of Natural Resources, Ontario (2009).** Controlling fox rabies in Ontario. <u>http://bit.ly/XzPI5q</u> (Accessed 23 January 2013).

¹⁹ De Benedictis, P., Gallo, T., Iob, A., Coassin, R., Squecco, G., Ferri, G., D'Ancona, F., Marangon, S., Capua, I. & Mutinelli, F. (2008). Emergence of fox rabies in north-eastern Italy. *Euro Surveill* **13**, 1-2. (p. 1)

²⁰ Vitasek, J. (2004). A review of rabies elimination in Europe. Vet Med (Praha) 49, 171-185.

²¹ See, e.g.: Schweiger, A., Ammann, R. W., Candinas, D., Clavien, P.-A., Eckert, J., Gottstein, B., Halkic, N., Muellhaupt, B., Prinz, B. M., Reichen, J., Tarr, P. E., Torgerson, P. R. & Deplazes, P. (2007). Human alveolar echinococcosis after fox population increase, Switzerland. *Emerg Infect Dis* **36**, 878-882.

²² E.g., **De Benedictis, P., et al. (2008).** *Ibid.* See also the searchable database presented by the Rabies Information System of the WHO Collaboration Centre for Rabies Surveillance and Research. <u>http://bit.ly/TmbwFZ</u> (Accessed 23 January 2013).

²³ For a useful account of the many disease threats to papayas, and the techniques of cultivation, see: Nishina, M., Zee, F., Ebesu, R., Arakaki, A., Hamasaki, R., Fukuda, S., Nagata, N., Chia, C. L., Nishijima, W., Mau, R. & Uchida, R. (2000). Papaya production in Hawaii. *Fruits and Nuts,* Cooperative Extension Service, University of Hawaii, June 2000, F&N-3, pp. 1-8 (especially pp. 6-7). For a picture of the complexity of management of multiple pests and diseases in the papaya crop, see: Constantinides, L. N. & McHugh, Jr., J. J. (eds.) (2008). *Pest Management Strategic Plan for Papaya Production in Hawaii*, University of Hawai'i at Mānoa.

²⁴ History from: Gonsalves, D. (2004). Transgenic papaya in Hawaii and beyond, *AgBioForum* 7, 36-40. Other valuable summaries are to be found in: Swain, S. & Powell, D. A. (2001). *Papaya Ringspot Virus Resistant Papaya: A Case Study,* Food Safety Network Technical Report; and Yoon, C. K. (1999). Stalked by Deadly Virus, Papaya Lives to Breed Again, *New York Times,* 20 July 1999. The Upjohn Company was involved in the project, see: US Department of Agriculture (2012). USDA Expands Export Opportunities for Hawaiian Rainbow Papaya. http://1.usa.gov/WfStvE (Accessed 23 January 2013).

²⁵ Gonsalves, D. (2004). *Ibid.*, p. 38.

²⁶ **Gonsalves, D. & Ferreira, S. (2003).** Transgenic papaya: A case for managing risks of Papaya ringspot virus in Hawaii. Online. *Plant Health Progress* doi:10.1094/PHP-2003-1113-03-RV, no page numbers.

²⁷ Japan export figure from: **Gonsalves, D. & Ferreira, S. (2003).** *Ibid.*

²⁸ Gonsalves, D. & Ferreira, S. (2003). *Ibid.* It remains unclear to what extent this plan was actually put into practice.

²⁹ Constantinides, L. N. & McHugh, Jr., J. J. (eds.) (2008). *Ibid.*, p. 11.

³⁰ Bondera, M. & Query, M. (2006). *Hawaiian Papaya: GMO Contaminated*, Hawaii SEED, p. 13. For an accounting of arguments against the GM papaya, see: **Valenzuela**, H. (2004). 'Rainbow' imperils other papayas. *Honolulu Advertiser*, 31 October 2004. <u>http://bit.ly/VrCKIp</u> (Accessed 23 January 2013).

³¹ US Department of Agriculture (2012). *Ibid.*

³² Papaya data from: **Economic Research Service, US Department of Agriculture (2011).** *Fruit and Tree Nut Yearbook*, Spreadsheet Files (89022), B-23, Table-B23.xlsx (Papayas: Acre, yield, production, utilization, and price, HI, 80-to date), <u>http://bit.ly/XY1xEw</u> (Accessed 23 January 2013). Inflation adjustment based on relative value performed with: <u>http://bit.ly/VWb2EK</u> (Accessed 23 January 2013).