

Update: Deployment of Innovative Genetic Vector Control Strategies including an update on the MosqGuide Project

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Abstract. This short note gives an update on the deployment of innovative genetic vector control strategies since the publication of the original paper in 2009. Rapid progress is being made in field activities with genetically modified *Aedes aegypti* that express a self-limiting trait. The process by which countries make decisions on risk assessment and management for GM mosquitoes within their national frameworks is an essential prerequisite to such field releases. This note also briefly updates on the activities of other initiatives described in the original paper, including the MosqGuide project.

Keywords: *Aedes aegypti*, Biosafety, Genetically modified mosquitoes, Risk assessment.

INTRODUCTION

Since the publication of Beech *et al.* (2009b) on “Deployment of Innovative Genetic Vector Control Strategies”, there has been rapid progress in the field of innovative genetic vector control strategies, in particular several supervised open field trials involving release of genetic strains (e.g. Simmons *et al.*, 2011; Harris *et al.*, 2011). To take advantage of this approach to vector control, some national biosafety authorities have taken decisions on open field release for the use of transgenic insects and other national authorities are in the process of reviewing applications for open field release. Many other initiatives described in the original paper have either concluded or have advanced to the next steps. It is therefore timely that the initiatives in the original paper are reviewed.

NATIONAL BIOSAFETY FRAMEWORKS

Brazil This country was used as an example in the original paper for the steps it had taken to consider specific applications of genetically modified insects within its existing regulatory framework for GMOs (Normative Resolution No7). The new regulation that covers GM insects (Normativa Insetos GM), and specifically GM mosquitoes which, as vectors of human disease, are classified at a higher biosafety level (NB2) than other insects, is still at the drafting stage at the time of writing. However, after presentation of a dossier, the National Biosafety Committee (CTNBio) took a decision

in December 2010¹ on a specific case – to allow the open field release of male “genetically sterile” *Aedes aegypti* carrying RIDL[®] (OX513A, Phuc *et al.*, 2007) traits at specific locations in the state of Bahia. The field release is to evaluate the ability of the RIDL strain to suppress a local population of wild-type *Aedes aegypti* at up to 5 sites for a period of 2 years. Annual reporting to CTNBio on release monitoring and suppression performance and biosafety compliance is required. Releases commenced in February 2011 and evaluation of the ability to suppress a local population is ongoing at the time of writing. Progress has been reported in a recently published paper (Oliveira *et al.*, 2011) and updates were shared in Portuguese on the social media site Twitter³ and the website of Moscamed, a not-for profit state organisation collaborating in the trials.

Malaysia The Malaysian Biosafety Act 2007, regulating GMOs in the environment, came into force in December 2009. Shortly afterwards a submission was made by the Institute for Medical Research in Kuala Lumpur to the National Biosafety Board (NBB) for a limited mark-release-recapture experiment of transgenic *Aedes aegypti* mosquitoes to determine dispersal and longevity in the environment.

The NBB, a committee that is administered via the Malaysian Ministry of Natural Resources and the Environment (NRE), took the decision in October 2010 (under the Biosafety Act 2007) to allow a small scale field release of ge-

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netically modified male sterile *Aedes aegypti* carrying RIDL® traits in both inhabited and uninhabited areas in the states of Pahang and Melaka⁴. A field release was conducted in December 2010 in an uninhabited forest area. Prior to the field release the trial was advertised in the national press on two separate occasions (5th and 19th Aug 2010) in both the national language (Bahasa Malaysia) and English, permission was obtained from local authorities and public meetings were held with local communities (Fong, 2011). Monitors from the NRE attended the release. NRE has taken great care to promote public awareness of the trials, through its website and requirements for public engagement criteria.

Before proceeding to the next phase of the trials in inhabited areas, NBB requirements included reporting of the uninhabited area results, compliance with biosafety conditions, and submission of a public engagement plan. It is anticipated that NRE will need to approve the public engagement plan prior to releases in inhabited areas commencing, even though the trial has already been authorised by NBB in their decision in October 2010.

Grand Cayman The Mosquito Research and Control Unit (MRCU) on Grand Cayman, Cayman Islands undertook open releases of RIDL *Aedes aegypti* in both 2009 and 2010 with approval from the Ministry of District Administration, Works, Lands and Agriculture (encompassing the Department of Environmental Health), and the Ministry of Health, Environment, Youth, Sports and Culture (including the Department of Environment). In addition to specific regulations governing import and use of insects in general and mosquitoes in particular, mainly specified in the Mosquito (Research and Control) Law (2007 Revision) and the Animal Law 2003, Cayman has a draft National Conservation Law which addresses the control of genetically modified organisms (GMOs). The trial was conducted in accordance with the provisions in the draft National Conservation Law. As part of the permitting process required in Grand Cayman for the import of the mosquitoes a risk assessment was required. As Cayman does not have a specified format for such a risk assessment a document was derived from relevant international risk assessment frameworks: Annex III of the Cartagena Protocol for Biosafety and the International Standard for Phytosanitary Measures on Pest Risk Analysis from the International Plant Protection Convention (IPPC). The risk assessment regarding the release of OX513A male *Aedes aegypti* that was performed on Grand Cayman has been placed into the public domain through the UK House of Lords, in response to a Parliamentary Question and is available online⁵.

The design and results of the trials have been submitted to peer-reviewed journals and should be available in the scientific literature in due course. The 2009 trials are described in Harris *et al.* (2011); a manuscript describing the 2010 trials has been submitted for publication.

Australia Australia has recently given permission for the field release of *Aedes aegypti* containing the intra-cellular bac-

terium, *Wolbachia*. This genetic strategy does not depend on the use of recombinant DNA technology and was therefore considered not subject to legislation governing the approval of genetically modified organisms in Australia; instead it was approved as a “Veterinary Chemical Product” through the Australian Pesticide and Veterinary Medicines Authority (APVMA). The regulatory path taken for the release of *Aedes aegypti* containing *Wolbachia*, which will sustain itself in the environment, has been described (De Barro *et al.*, 2011) and includes a published risk assessment (Murphy *et al.*, 2010), albeit of a strain of *Wolbachia* different from that released. Further updates on this project can be obtained at the eliminatedengue.com website⁶ and from recently published papers (Hoffman *et al.*, 2011, Iturbe-Ormaetxe *et al.*, 2011, Walker *et al.*, 2011).

INTERNATIONAL ACTIVITIES

Cartagena Biosafety Protocol

The Ad Hoc Technical Group on Risk Assessment and Risk Management (AHTEG) has concluded their initiative to gather information on risk assessment and risk management of living modified mosquitoes (LMM) in accordance with Annex III of the Cartagena Biosafety Protocol. The document was noted at the COP-MOP 5 meeting in Nagoya, Japan in November 2010 and is available on the Biosafety Clearing House web site (Ad Hoc Technical Expert Group on Risk Assessment and Risk Management (AHTEG), 2010), but further scientific reviewing and testing to establish its overall utility and applicability to living modified organisms of different taxa introduced into different environments was requested by the Members⁷. The document recommends four specific aspects to be considered during the risk assessment for GM mosquitoes:

- **Effects on biological diversity** including habitat range, invasive or native species, interactions with predators and prey species and potential effects on ecosystem services.
- **Gene flow**, including vertical, horizontal and persistence in the environment.
- **Evolutionary responses** including avoidance strategies and vector competence.
- **Risk management strategies** including management of resistance, release strategies, quality control of released mosquitoes, and monitoring in the environment.

WHO/TDR initiatives

MosqGuide The World Health Organization Special Program in Research and Training in Tropical Diseases (WHO/TDR) funded project, “Best Practice Guidance for Deployment of Genetic Control Methods against Mosquito Vec-

tors in Disease Endemic Countries” (MosqGuide) is preparing and validating guidance for support and decision making as well as ethical, social and cultural issues regarding the deployment of GM mosquitoes. The project was described in Mumford *et al.* (2009). Although the project itself is not involved with field release of GM mosquitoes, individual partners in the project have observed or participated in recent field activities in Malaysia, Brazil and Grand Cayman. For example, members of the project team have led activities including community engagement for the release of sterile male mosquitoes in Bahia, Brazil (Oliveira *et al.*, 2011). In Panama in 2009 the project brought expertise and experience from Mexico, Brazil, Thailand and the UK as resource experts for the first consultation amongst the scientific, regulatory and vector control communities (to complement actions by the national research institution, the Gorgas Memorial Institute of Tropical and Preventative Medicine, considering GM mosquito research and trials) in 2009. The MosqGuide website (www.mosqguide.org.uk) features reports, presentations and articles addressing key considerations for decision making on GM vectors, whilst conclusions about acceptable risk for the predicted benefits should be determined on a case by case basis. MosqGuide uses a modular approach and several of its outputs are available online. Materials are regularly being uploaded to the MosqGuide website as they become available.

MosqGuide has prepared a description of genetic vector technology and a comprehensive bibliography on the techniques and other relevant matters such as risk assessment. These documents form part of Module 1. Module 2 (research considerations) has been finalised and is available on the MosqGuide website and Module 3 (National Decision making) was discussed and validated with some national regulators at a workshop conducted at the International Society for Biosafety Research meeting on Genetically Modified Organisms in Argentina in November 2010 (ISBGMO, 2010). A draft of Module 4 is also available on the website which discusses the data that might be required for decision making. Module 6 is described below (Capacity Building) as it was developed in conjunction with the WHO/TDR funded regional training course curricula on genetically modified vectors. Updates on Module 5, regarding stakeholder involvement, and Module 7, a computer based prototype decision support tool are forthcoming.

MosqGuide also regularly publishes a newsletter, which collates public domain information regarding dengue, malaria, genetically modified vectors, biotechnology policies and other relevant information. The newsletter has an approximate circulation of 100 individuals across the globe, and back issues are archived on the MosqGuide website (<http://www.mosqguide.org.uk/newsletters.htm>).

Other national and international initiatives have also been discussed (Beech *et al.*, 2009b; Mumford *et al.*, 2009). Further technical and ethical/social/regulatory support will be provided by the project team as the consultation moves to public interest groups, environmentalists and other stakeholders in 2011/2012.

The WHO/TDR and the Foundation for the National Institutes for Health (FNIH) have convened a Working Group on GM Mosquitoes to follow up the recommendations of the Technical Consultation on GM Mosquitoes held at WHO in May, 2009 (World Health Organization, 2010). This group’s report on safety, efficacy, ethical and regulatory issues related to GM mosquitoes is currently under peer review and is proposed for publication in late 2011 or early 2012.

Capacity Building The WHO/TDR funded regional training centres for genetically modified vectors continued to run courses in 2010 in all three regional centres in Africa, Asia and Latin America, increasing the awareness and knowledge of genetically modified vectors for additional participants. Courses were held in Mali in September 2010, and in India and Colombia in November 2010. The courses in Mali and India were the third and final training courses for those centres. One specific outcome of the second Asian training course held in India in 2010 was a re-evaluation of a paper published by Beech *et al.* (2009a) on “Risk analysis of a hypothetical open field release of a self-limiting transgenic *Aedes aegypti* mosquito strain to combat dengue”. The group re-examined the risks identified in the original paper and identified two additional risks for a bi-sex lethal RIDL strain: the presence of tetracycline in the environment and the multiple mating of wild females with sterile or wild males, both of which might affect the efficacy of the SIT programme (Patil *et al.*, 2010). The group also looked at the potential risks involved in the release of a strain of GM *Aedes aegypti* with a specific female flightless phenotype. Module 6 of MosqGuide consists of curricula developed for the courses run in the three regional training centres and permissions are being sought to add it to the MosqGuide website. The course participants have developed informal networks, through the use of social networking tools and email and are kept informed of information regarding the research, development and use of GM vectors through the circulation of the MosqGuide Newsletters, which as previously stated are archived on the MosqGuide website.

REGIONAL ACTIVITIES

European Food Safety Authority (EFSA)

Beech *et al.* (2009b) identified additional initiatives for the risk assessment, management and communication on GM insects. One of these was the regional initiative in the European Union (EU) for Environmental Risk Assessment Criteria for Genetically Modified (GM) Insects to be placed on the EU Market. EFSA launched a tender for a report on the topic which was won by a consortium including the Environment Agency Austria, the International Atomic Energy Agency and the University of Bern. The resulting document (Benedict *et al.*, 2010) looked at GM arthropods of

relevance to the EU, in a timeframe of the next 10 years, and identified potential hazards and possible methods for their evaluation as well as the severity and likelihood to become a risk. Assessment endpoints were also defined. Issues considered relevant for the Environmental Risk assessment of GM insects in the EU context were summarised as:

- **Issues relating to the parental organism;** indigenous or alien organism, habitat range, known pest species or biocontrol agent, host range, mobility, interactions with conservation species and any current control methods.
- **Issues relating to the genetic modification;** nature and function of inserted transgenes, stability of the genetic modification, transformation system, site and level of gene expression.
- **Issues relating to the GM arthropod;** changes to reproduction, survival and fitness, mobility, composition and phenotype, behaviour, ecological services, vector competence, reactions to biotic and abiotic stress, ability to control the organism with alternative means.
- **Issues relating to the environment and release characteristics;** availability of cross compatible wild relatives, factors affecting dispersal, release numbers, mechanisms and locations.

Key considerations also included the collection of baseline data, the choice of the comparator against which the GM arthropod should be evaluated, as well as a case by case consideration of potential risk. EFSA is now following up this report, together with similarly commissioned reports on GM fish and GM mammals and birds, with a series of Working Groups which will compile a Guidance document on GM animals, encompassing each of these taxonomic groups. This will complement the existing EFSA Guidance for GM plants⁸, and should be completed during 2012, after public consultation.

ETHICAL, SOCIAL AND CULTURAL (ESC) DIMENSIONS

It is vital that both researchers and regulators involved with research and development activities of GM mosquitoes are able to effectively communicate risks and benefits to key stakeholders and have the skills to interact with the media in an open and constructive way. Three initiatives were identified in the original paper regarding ESC aspects of research and development with GM mosquitoes. The first of these was a risk communication workshop that took place in Kuala Lumpur, Malaysia, in early 2010 sponsored by the United Nations Development Programme and University of Malaya (described below). Over 39 participants representing scientists, regulators and other stakeholders participated in risk communication activities. The second was a public engagement meeting that took place in Panama in October, 2009 (also described below). The third initiative was ESC activities conducted for Grand Challenges in Global Health (GCGH) projects. Recent publications from the GCGH

projects include those involved with the field release of *Aedes aegypti* infected with *Wolbachia* strains ((McNaughton *et al.*, 2010) and a proposal for an overall framework for community engagement in public health research (Lavery *et al.*, 2010).

Kuala Lumpur meeting – Identifying key stakeholders and communicating risk In March 2010 a three day UNDP-sponsored workshop on Risk Communication was organised in Selangor, Malaysia. Participants, consisting of scientists, regulators and other stakeholders in Malaysia, worked on group activities aimed at arming them with basic skills in risk communication. The event was timed and structured so that as the development of transgenic insects neared the stage of field trials and eventual open release in Malaysia they would be able to communicate potential benefits and risks associated with the technologies to all key stakeholders. Lectures covered the technologies involved in producing useful transgenic insects, theories of Risk Communication (Fischhoff, 1995; Slovic, 1987), understanding the media and developing good interview techniques. Group activities included practicing ‘elevator pitches’, media interviews and press conferences, and discussion on communication of potential risks in the context of two hypothetical case studies. There was broad agreement between groups in identifying the most important stakeholders to whom the risks needed to be communicated, though prioritisation differed between groups. The suggested means to communicate the proposed risks to the relevant stake holders included stating clearly that they were ‘not scientifically possible’, and pointing to laboratory studies, particularly peer-reviewed publications, as evidence that a risk has not been seen to materialise thus far, giving clear facts to explain why the risks were not great and providing assurance that more studies would be conducted to examine risks further.

Panama meeting – ESC aspects In October 2009, the Gorgas Memorial Institute of Tropical and Preventive Medicine and representatives of the Ministry of Health (MINSa) of Panama hosted a one day meeting on “Use of New Alternatives for the Control of Mosquito Vectors of Diseases” (in Spanish) held in Panama City, Panama. The invited experts from national, regional and international bodies, presented the state of the art on area-wide control of mosquitoes, using examples from irradiated releases (Italy and in planning for Sudan) and GM mosquito releases (pending in Malaysia at that time). There was also an overview of Panama’s experience with area-wide control of other insect pests and the rising threat of dengue as a disease now considered endemic in the region. The head of the Department for Vector Control explained their recently enhanced practices in outbreak response. In addition to plenary presentations and question/answer sessions, there were breakout sessions to facilitate discussion in the context of possible employment of a GM strategy. The two groups focused on ethical, social and cultural issues and community participation, and biosafety issues and regulation. In the latter case, the concurrent im-

provement of the National Biosafety Framework was lauded by those who had attempted to gain approval for import of GM insects through the previous, far less transparent system.

This meeting was aimed at the scientific and technical community, although publicised to the press to attract other interested parties. Some technical questions regarding area-wide control of insects and on genetic modification were addressed. However, feedback from the participants was overwhelmingly focused on taking advantage of the best options for controlling dengue. The sense that new methods for vector control are needed was only qualified with a concern that the affected communities could view any novel technique as a “silver bullet” and, as a result, stop what little participation has been gained from years of promoting individual and community actions (e.g. removing sites with standing water). Subsequent to this first broad discussion, the Gorgas Institute – the research and advisory body for the Ministry of Health on such issues – has continued to explore the option of a genetic strategy for control of the dengue vector, with a grant from the Panamanian government building on very preliminary planning for phased testing, which was supported by the TDR earlier in 2009.

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REFERENCES

- Ad Hoc Technical Expert Group on Risk Assessment and Risk Management (AHTEG) 2010. Risk Assessment of Living Modified Mosquitoes. In: Convention on Biological Diversity (ed.) Guidance on Risk Assessment of Living Modified Organisms. Montreal: Secretariat on the Convention on Biological Diversity, United Nations Environmental Programme.
- Beech, C., Nagaraju, J., Vasana, S., Rose, R., Othman, R., Pillai, V. and Saraswathy, T. 2009a. Risk analysis of a hypothetical open field release of a self-limiting transgenic *Aedes aegypti* mosquito strain to combat dengue. *Asia Pacific Journal of Molecular Biology and Biotechnology* 17(3): 97-108.
- Beech, C., Vasana, S., Quinlan, M., Capurro, M. L., Alphey, L., Bayard, V., Bouare, M., McLeod-Corena, M., Kitayapong, P., Lavery, J., Lee, H. L., Marelli, M., Ombongi, K., Othman, R. Y., Pillai, V., Ramsey, J., Reuben, R., Rose, R. I., Tyagi, B. K. and Mumford, J. 2009b. Deployment of innovative genetic vector control strategies: Progress on Regulatory and Biosafety Aspects, Capacity Building and Development of Best Practice Guidance. *Asia Pacific Journal of Molecular Biology and Biotechnology* 17(3): 75-85.
- Benedict, M., Eckerstorfer, M., Franz, G., Gaugitsch, H., Greiter, A., Heissenberger, A., Knols, B., Kumschick, S., Nentwig, W. and Rabitsch, W. 2010. Defining Environmental Risk Assessment Criteria for Genetically Modified Insects to be placed on the EU Market. Environment Agency Austria (Umweltbundesamt).
- De Barro, P., Murphy, B., Jansen, C. and Murray, J. 2011. The proposed release of the yellow fever mosquito, *Aedes aegypti*, containing a naturally occurring strain of *Wolbachia pipiensis*, a question of regulatory responsibility. *Journal für Verbraucherschutz und Lebensmittelsicherheit* (Journal for Consumer Protection and Food Safety), 6 (suppl 1), S33-S40.
- Fischhoff, B. 1995. Risk perception and communication unplugged: Twenty years of progress. *Risk Analysis* 15(2): 137-145.
- Fong, L. 2011. Over 200 people attended GM mozzie trials, says IMR official. The Star Online, 31 January 2011.
- Harris, A., Nimmo, D., McKemey, A., Kelly, N., Scaife, S., Donnelly, C.A., Beech, C., Petrie, W. and Alphey, L. 2011. Field performance of engineered male mosquitoes. *Nature Biotechnology* 29(11): 1034-1037.
- Hoffman, A., Montgomery, B., Popovici, J., Irurbe-Ormaetxe, I., Johnson, P.H., Muzzi, F., Greenfield, M., Durkan, M., Leong, Y., Dong, Y., Cook, H., Axford, J., Callahan, A.G., Kenny, N., Omodel, C., McGraw, E.A., Ryan, P.A., Ritchie, S., Turelli, M. and O'Neill, S. 2011. Successful establishment of *Wolbachia* in *Aedes* populations to suppress dengue transmission. *Nature* 476: 454-456.
- ISBGMO. 2010. The Role of Biosafety Research in the Decision Making Process Proceedings of the 11th International Symposium on the Biosafety of Genetically Modified Organisms. In: 11th International Symposium on the Biosafety of Genetically Modified Organisms (ISBGMO), Buenos Aires, Argentina.
- Iturbe-Ormaetxe, I., Walker, T. and O'Neill, S. 2011. *Wolbachia* and the biological control of mosquito-borne disease. *EMBO Reports* 12 (6): 508-518.
- Lavery, J., Tinadana, P.O., Scott, T.W., Harrington, L., Ramsey, J., Ytuarte-Núñez, C., and James, A. 2010.

- Towards a framework for community engagement in global health research. *Trends in Parasitology* 26(6): 279-83.
- McNaughton, D., Clough, A., Johnson, P., Ritchie, S. and O'Neill, S. 2010. Beyond the back yard: Lay knowledge about *Aedes aegypti* in northern Australia and its implications for policy and practice. *Acta Tropica* 116: 74-80.
- Mumford, J., Quinlan, M., Beech, C.J., Alphey, L., Bayard, V., Capurro, M.L., Kittayapong, P., Knight, J.D., Marrelli, M.T., Ombongi, K., Ramsey, J.M. and Reuben, R. 2009. MosqGuide: A project to develop best practice guidance for the deployment of innovative genetic vector control strategies for malaria and dengue *Asia Pacific Journal of Molecular Biology and Biotechnology* 17(3): 93-95.
- Murphy, B., Jansen, C., Murray, J. and DeBarro, P. 2010. Risk Analysis on the Australian Release of *Aedes aegypti* (L.)(Diptera: Culicidae) containing *Wolbachia*. CSIRO.
- Oliveira, S.L.O., Carvalho, D.O. and Cappurro, M.L. 2011. Mosquito transgenico: do paper para realidade (Transgenic mosquito: from paper to reality). *Revista de Biologia* 6b: 38-43.
- Patil, P., Alam, M., Ghimire, P., Lacroix, R., Kusumawathie, P., Chowdhury, R., Sunish, I., Libo, X., Vu, P., Aung, M., Burneebaatar, B., Thanispong, K., Dharamsingh, D. and KHAN, A. 2010. Discussion on the proposed hypothetical risks in relation to open field release for a self-limiting transgenic *Aedes aegypti* mosquito strain to combat dengue. *Asia Pacific Journal of Molecular Biology and Biotechnology* 18(2): 241-246.
- Slovic, P. 1987. Perception of Risk. *Science* 236: 280-285.
- Walker, T., Johnson, P.H., Moreira, L., Iturbe-Ormaetxe, I., Frentiu, F.D., McMeniman, M., Leong, Y., Dong, Y., Axford, J., Kreisner, P., Lloyd, A., Ritchie, S., O'Neill, S. and Hoffman, A. 2011. The wMel *Wolbachia* strain blocks dengue and invades caged *Aedes aegypti* populations. *Nature* 476: 450-453.
- World Health Organization. 2010. Progress and prospects for the use of genetically modified mosquitoes to inhibit disease transmission. WHO, Geneva, Switzerland. 64pp. [Accessed 13 June 2011].
- inant autosomal conditional lethal genetic system". However, this is rather cumbersome, so we tend to use the shorthand of "sterile", by analogy with radiation-sterilisation, which has a similar overall effect of leading to the death of some or all progeny of a "sterile" male. See Alphey et al (2010).
- ³ <http://twitter.com/#!/moscamed> [Accessed 5 Oct 2011].
- ⁴ Malaysian government opinion on open release of GM mosquitoes: <http://bch.cbd.int/database/record-v4.shtml?documentid=101480> [Accessed 13 June 2011].
- ⁵ <http://www.parliament.uk/deposits/depositedpapers/2011/DEP2011-0053.pdf> [Accessed 08 July 2011].
- ⁶ <http://eliminatedengue.com/en/HOME.aspx> [accessed 3 October 2011].
- ⁷ <http://www.cbd.int/decision/mop/?id=12325> [accessed 12 October 2011].
- ⁸ <http://www.efsa.europa.eu/it/scdocs/doc/1879.pdf> [Accessed 13 June 2011].

FOOTNOTES

¹ <http://www.jusbrasil.com.br/diarios/23935599/dou-secao-1-17-12-2010-pg-48> [Accessed 13 June 2011]

² A more precise term would be "heritable single-locus dom-