



Summary of the Risk Assessment and Risk Management Plan for Licence Application DIR 183

Decision

The Gene Technology Regulator (the regulator) has decided to issue a licence (DIR 183) to allow the Westmead Institute for Medical Research to conduct a clinical trial to evaluate the safety and efficacy of genetically modified (GM) *E.coli* to deliver genes that restore sensitivity to antibiotics in gut bacteria.

Clinical trials conducted in Australia must be conducted in accordance with the National Statement on Ethical Conduct in Human Research and with the Guidelines for Good Clinical Practice of the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.

The Regulator has prepared a Risk Assessment and Risk Management Plan (RARMP) for this application, which concludes that the proposed clinical trials pose negligible risks to human health and safety and the environment. Licence conditions have been imposed for the proposed clinical trial to manage any risk posed by the dealings.

The application

Application number	DIR 183
Applicant	The Westmead Institute for Medical Research
Project title	Clinical trial with genetically modified <i>E.coli</i> to reduce antibiotic resistance
Parent organism	<i>Escherichia coli</i> (Nissle strain) and human gut bacteria
Introduced gene and modified trait	Two antibiotic resistance plasmids (circular pieces of bacterial DNA) were modified by <ul style="list-style-type: none">• Deletion of genes responsible for resistance to multiple classes of antibiotics• Deletion of genes that enable plasmids to persist in bacteria• Introduction of genes for resistance to specific antibiotics (fosfomycin or tetracycline) to enable selection for the GMO
Previous releases / approvals	First in human trial
Proposed locations	Westmead hospital
Primary purpose	The proposed trial is designed to evaluate the safety and efficacy of GM <i>E.coli</i> to deliver genes to gut bacteria that restore sensitivity to antibiotics

Risk assessment

The risk assessment concludes that risks to the health and safety of people or the environment from the proposed clinical trial are negligible. No specific risk treatment measures are required to manage these negligible risks.

The current assessment focuses on risks posed to people other than the intended treatment recipient and to the environment, including long term persistence of the GMOs, which may arise from the administration and disposal of the GMO.

The risk assessment process considers how the genetic modifications and activities conducted with the GMO might lead to harm to people or the environment. Risks are characterised in relation to both the seriousness and likelihood of harm, taking into account information in the application (including proposed controls), relevant previous approvals, current scientific/technical knowledge and advice received from a wide range of experts, agencies and authorities. Both the short and long term risks were considered.

Credible pathways to potential harm that were considered included: whether people and animals can be inadvertently exposed to the GMO, and the potential for transfer of genetic material to and from the GMO. The potential for GMO to be released into the environment and its effects was also considered.

The principal reasons for the conclusion of negligible risks are that the potential risks that could arise would be the result of genetic recombination and transmission events that are unlikely to occur given the limits and controls imposed.

Risk management plan

The risk management plan describes measures to protect the health and safety of people and to protect the environment by controlling or mitigating risk. The risk management plan is given effect through licence conditions.

As the level of risk is considered negligible, specific risk treatment is not required. However, since this is a clinical trial, the licence includes limits on the number of trial participants, location limited to hospitals and clinical trial sites, limits on the duration of the trial, as well as a range of controls to minimise the potential for the GMO to spread to non-participants. In addition, there are several general conditions relating to ongoing licence holder suitability, auditing and monitoring, and reporting requirements which include an obligation to report any unintended effects.