Horizontal Gene Transfer Field Trials

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Based on the paper...

EVALUATION OF HORIZONTAL GENE TRANSFER MONITORING EXPERIMENTS CONDUCTED IN NEW ZEALAND BETWEEN 2004 AND 2009
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Key messages

1. INBI found that the monitoring of HGT in soil was superficial and fundamentally flawed for purpose

2. Guidance is needed for evaluating risks of LMOs that may involve microorganisms and/or LM microorganisms

3. INBI encourages governments to endorse an extension of the AHTEG with a mandate to develop guidance on microorganisms

What was the regulatory issue?

2002 the developer received regulatory permission for contained field trial of cows genetically engineered with genes of human origin

Regulator imposes conditions, e.g.,:

- Limits on the kinds of DNA that could be used in the making of GM bovine; and
- "Micro-organisms shall be tested for the presence of the introduced genetic modifications at the disposal sites. If HGT is detected, genetic modification and disposal of cattle shall be immediately halted"
Main point to regulator

“HGT is defined as the transfer of genetic material from one organism to another organism outside the context of parent to offspring (i.e. vertical) reproduction” (p. 1 ERMANZ 2006).

Regulator: “significant uncertainty as to the magnitude and likelihood of the adverse effect arising”

“The applicant will monitor for HGT at the disposal sites and in the event of HGT being detected the project will be halted and a remediation plan developed (control 6.4)”

“[w]ith these controls in place, the combined non-negligible risks referred to above are considered to be low, even after taking account of uncertainty”

What was monitored?: bacteria

Culturable, aerobic bacteria: 0.1-1% of soil bacteria

Only antibiotic resistant bacteria

No eukaryotes (e.g., fungi)

“It is now widely accepted that HGT occurs, most significantly within the prokaryote kingdom, but instances of nucleic acid transfer between prokaryotes and eukaryotes are documented in the scientific literature” (p. 24 ERMANZ, 2002).
1 gram of soil has ~2 billion bacteria

Not all HGT conserves target

Table 2. Calculated total scale of AgResearch survey to inform risk assessment and risk management of HGT.

<table>
<thead>
<tr>
<th>Report</th>
<th>Number of bacteria screened by probe</th>
<th>Maximum equivalent of soil surveyed (g) (x 10⁷)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Pit</td>
</tr>
<tr>
<td>2004</td>
<td>512</td>
<td>648</td>
</tr>
<tr>
<td>2007</td>
<td>338</td>
<td>349</td>
</tr>
<tr>
<td>2009a</td>
<td>249</td>
<td>250</td>
</tr>
<tr>
<td>2009b</td>
<td>251</td>
<td>251</td>
</tr>
<tr>
<td>Cumulative total weight of soil surveyed 2004-2009</td>
<td>17.4 µg</td>
<td></td>
</tr>
</tbody>
</table>

* Based on estimated 2 x 10⁸ bacteria per gram of soil. Sum of control and pit.
Monitoring plan

Minimum depth MAF Standard 154.03.06

Possible depth

Pit management

Which pits were sampled?

Were they sampled more than once?

How long after cows introduced were they sampled?
To scale of average human

Conclusions

Developer: “no evidence” of HGT.

INBI: Given the context, that these experiments were performed for the purpose of increasing our knowledge of the risks and safety of transgenes used in GM animals, this claim comes with the responsibility of demonstrating that the negative result (that is, the absence of detectable gene transfer) has scientific meaning.
Conclusions

Developer: “no evidence” of HGT.

INBI: failure to discuss the limits of the detection experiments. Limits of detection in sampling and in molecular work.

The molecular series was composed of largely unfinished experiments. Negative results were left unchallenged when simple and routine controls could have added confidence to the findings.

What could be done?

HGT risk assessment/monitoring is difficult!
Assessment science has not significantly advanced in biosafety literature since 1990s
Has advanced in research literature:
  • Metagenomics (high throughput)
  • Microcosm experiments to test conditions/assumptions and provide power analysis
  • Concentrators: where would the products of HGT accumulate? e.g., worm guts (see Hart 2009)
  • Mutators: who is most likely to acquire genes by HGT?