Australian Government
Department of Health and Ageing
Office of the Gene Technology Regulator

Guidance tables on the changes to the classification of contained dealings with viral vectors resulting from the implementation of the *Gene Technology Amendment Regulations 2011 (No. 1)**

Table 1. Dealings with replication competent vectors

Characteristics of the vector	Characteristics of donor nucleic acid (transgene)	Characteristics of the dealings			
		In vitro		*In vivo*	
		Regulations as amended July 2007	Regulations as amended Sept 2011*	Regulations as amended July 2007	Regulations as amended Sept 2011*
Any virus which meets the criteria of a Risk Group 4 microorganism in AS/NZS 2243.3:2010 with any genetic modification		Not differentiated from below	DNIR 3.1(p)	Not differentiated from below	DNIR 3.1(p)
Any replication competent vector	Toxin or uncharacterised gene from toxin producing organism	DNIR 3.1 (a), (b) or (c)			
	Genes whose expressed products are likely to increase the capacity of the virus/viral vector to induce an autoimmune response	DNIR 3.1 (g)	DNIR 3.1 (h)	DNIR 3.1 (g)	DNIR 3.1 (h)
	Creates novel replication competent virus with altered host range or mode of transmission, or increased virulence, pathogenicity or transmissibility	DNIR 3.1 (h)	DNIR 3.1 (i)	DNIR 3.1 (h)	DNIR 3.1 (i)
Non-pathogenic plant virus Or Baculovirus (*Autographa californica nuclear polyhedrosis virus*), polyhedrin minus	Not a toxin and not a pathogenic determinant and not an oncogenic modification	exempt (PC2 NLRD 2.1 (f) if > 25L)	exempt (PC2 NLRD 2.1 (f) if > 25L)	PC2 NLRD 2.1 (c)	
	Oncogenic modification	PC1 NLRD 1.1(b)	Exempt (PC2 NLRD 2.1 (f) if > 25L)		
	Pathogenic determinant	PC2 NLRD 2.1(e)		DNIR 3.1 (f)	DNIR 3.1 (g)
All others (now including Avipox vectors)	Not a toxin and not a pathogenic determinant and not an oncogenic modification and not immunomodulatory in humans	PC2 NLRD 2.1 (c) or (d)			
	Oncogenic modification or immunomodulatory in human	DNIR 3.1(d)	DNIR 3.1(e)	DNIR 3.1(d)	DNIR 3.1(e)
	Pathogenic determinant	DNIR 3.1 (e) or (f)	DNIR 3.1 (f) or (g)	DNIR 3.1 (e) or (f)	DNIR 3.1 (f) or (g)
	Drug resistance genes or other nucleic acid that could impair practical treatment of any disease or abnormality caused by the viral vector	DNIR 3.1 (n)	DNIR 3.1 (o)	DNIR 3.1 (n)	DNIR 3.1 (o)

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Table 2. Dealings with replication defective[1] retroviral vectors

Characteristics of the vector			Characteristics of donor nucleic acid (transgene)	Characteristics of the dealings			
				In vitro		*In vivo*	
Able to transduce human cells	SIN[2]	Accessory genes present[3]		Regulations as amended July 2007	Regulations as amended Sept 2011*	Regulations as amended July 2007	Regulations as amended Sept 2011*
Yes or no	Yes or no	Yes or no	Toxin or uncharacterised gene from toxin producing organism	DNIR 3.1 (a), (b) or (c)			
			Genes whose expressed products are likely to increase the capacity of the virus/viral vector to induce an autoimmune response	DNIR 3.1 (g)	DNIR 3.1 (h)	DNIR 3.1 (g)	DNIR 3.1 (h)
			Creates novel replication competent virus with altered host range or mode of transmission, or increased virulence, pathogenicity or transmissibility	DNIR 3.1 (h)	DNIR 3.1 (i)	DNIR 3.1 (h)	DNIR 3.1 (i)
No	Yes or no	Yes or no	Not a toxin and not a pathogenic determinant and not an oncogenic modification and not immunomodulatory in humans	exempt (PC2 NLRD 2.1 (f) if > 25L)		PC2 NLRD 2.1 (c) & (d)	PC2 NLRD 2.1 (i)
			Immunomodulatory in humans			DNIR 3.1 (d)	
			Oncogenic modification	PC1 NLRD 1.1 (b)	exempt (PC2 NLRD 2.1 (f) if > 25L)		
			Pathogenic determinant	PC2 NLRD 2.1 (e)		PC2 NLRD 2.1 (c) & (d)	
Yes	Yes	No	Not a toxin and not an oncogenic modification and not immunomodulatory in humans	PC2 NLRD 2.1 (i)	PC2 NLRD 2.1 (l)	PC2 NLRD 2.1 (d)	PC2 NLRD 2.1 (m)
			Oncogenic modification or immunomodulatory in human			DNIR 3.1 (d)	DNIR 3.1 (d) & (j)
		Yes	Not a toxin and not an oncogenic modification and not immunomodulatory in humans	DNIR 3.1 (i)	PC2 NLRD 2.1 (l)	DNIR 3.1 (i)	PC2 NLRD 2.1 (m)
			Oncogenic modification or immunomodulatory in human	DNIR 3.1 (d) & (i)		DNIR 3.1 (d) & (i)	DNIR 3.1 (d) & (j)
	No	No	Not a toxin and not an oncogenic modification and not immunomodulatory in humans	Lentiviral: DNIR 3.1 (i)	PC2 NLRD 2.1 (l)	Lentiviral: DNIR 3.1 (i)	PC2 NLRD 2.1 (m)
				other: PC2 NLRD 2.1 (i)		other: PC2 NLRD 2.1 (i)	
			Oncogenic modification or immunomodulatory in human	Lentiviral: DNIR 3.1 (i)		DNIR 3.1 (d) & (i)	DNIR 3.1 (d) & (j)
				other: PC2 NLRD 2.1 (i)			
		Yes	Not a toxin and not an oncogenic modification and not immunomodulatory in humans	DNIR 3.1 (i)	DNIR 3.1 (j)	DNIR 3.1 (i)	DNIR 3.1 (j)
			Oncogenic modification or immunomodulatory in human	DNIR 3.1 (d) & (i)	DNIR 3.1 (d) & (j)	DNIR 3.1 (d) & (i)	DNIR 3.1 (d) & (j)

[1] Replication defective retroviral vectors must include safety features to reduce the likelihood of recombination leading to replication competence being regained, including that all viral genes must be removed from the retroviral vector so that it cannot replicate or assemble into a virion without these functions being supplied *in trans*, and that viral genes needed for virion production must be expressed from independent, unlinked loci with minimal sequence overlap

[2] Indicates the presence of a 'self inactivating' deletion in the unique 3' region of the long terminal repeat (LTR) that eliminates the LTR promoter activity after integration of the provirus into the host genome

[3] Only *gagpol*, *env* (and *rev* if a lentiviral vector) present in the packaging system

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Table 3. Dealings with replication defective non-retroviral vectors

<table>
<tr><th rowspan="3">Characteristics of the vector</th><th rowspan="3">Characteristics of the donor nucleic acid (transgene)</th><th colspan="4">Characteristics of the dealings</th></tr>
<tr><th colspan="2">In vitro</th><th colspan="2">In vivo</th></tr>
<tr><th>Regulations as amended July 2007</th><th>Regulations as amended Sept 2011*</th><th>Regulations as amended July 2007</th><th>Regulations as amended Sept 2011*</th></tr>
<tr><td colspan="2">Any viral vector derived from a virus which meet the criteria of a Risk Group 4 microorganism in AS/NZS 2243.3:2010 with any donor nucleic acid</td><td>Not differentiated from below</td><td>DNIR 3.1(p)</td><td>Not differentiated from below</td><td>DNIR 3.1(p)</td></tr>
<tr><td rowspan="3">All replication defective non-retroviral vectors, able or not able to transduce human cells</td><td>Toxin or uncharacterised gene from toxin producing organism</td><td colspan="4">DNIR 3.1 (a), (b) or (c)</td></tr>
<tr><td>Genes whose expressed products are likely to increase the capacity of the virus/viral vector to induce an autoimmune response</td><td>DNIR 3.1 (g)</td><td>DNIR 3.1 (h)</td><td>DNIR 3.1 (g)</td><td>DNIR 3.1 (h)</td></tr>
<tr><td>Creates novel replication competent virus with altered host range or mode of transmission, or increased virulence, pathogenicity or transmissibility</td><td>DNIR 3.1 (h)</td><td>DNIR 3.1 (i)</td><td>DNIR 3.1 (h)</td><td>DNIR 3.1 (i)</td></tr>
<tr><td rowspan="4">Not able to transduce human cells</td><td>Not a toxin and not a pathogenic determinant and not an oncogenic modification and not immunomodulatory in humans</td><td colspan="2" rowspan="2">exempt
(PC2 NLRD 2.1 (f) if > 25L)</td><td>PC2 NLRD 2.1 (c) & (d)</td><td rowspan="3">PC2 NLRD 2.1 (i)</td></tr>
<tr><td>Immunomodulatory in humans</td><td rowspan="2">DNIR 3.1 (d)</td></tr>
<tr><td>Oncogenic modification</td><td>PC1 NLRD 1.1 (b)</td><td>exempt (PC2 NLRD 2.1 (f) if > 25L)</td></tr>
<tr><td>Pathogenic determinant</td><td colspan="2">PC2 NLRD 2.1 (e)</td><td>PC2 NLRD 2.1 (c) & (d)</td></tr>
<tr><td rowspan="4">Able to transduce human cells,
Human adenovirus or
Adeno associated virus</td><td>Not a toxin and not an oncogenic modification and not immunomodulatory in humans</td><td colspan="2">PC1 NLRD 1.1 (c)</td><td>PC2 NLRD 2.1 (d)</td><td>PC2 NLRD 2.1 (k)</td></tr>
<tr><td>Immunomodulatory in humans</td><td>PC1 NLRD 1.1 (c)</td><td rowspan="2">PC2 NLRD 2.1 (j)</td><td colspan="2" rowspan="2">DNIR 3.1 (d)</td></tr>
<tr><td>Oncogenic modification</td><td>PC2 NLRD 2.1 (i)</td></tr>
<tr><td>Drug resistance genes or other nucleic acid that could impair practical treatment of any disease or abnormality caused by the viral vector</td><td>DNIR 3.1 (n)</td><td>DNIR 3.1 (o)</td><td>DNIR 3.1 (n)</td><td>DNIR 3.1 (o)</td></tr>
<tr><td rowspan="4">Able to transduce human cells
(other viruses)</td><td>Not a toxin and not oncogenic modification and not immunomodulatory in humans</td><td rowspan="3">PC1 NLRD 1.1 (c)</td><td rowspan="3">PC2 NLRD 2.1 (j)</td><td>PC2 NLRD 2.1 (d)</td><td>PC2 NLRD 2.1 (k)</td></tr>
<tr><td>Immunomodulatory in humans</td><td colspan="2" rowspan="2">DNIR 3.1 (d)</td></tr>
<tr><td>Oncogenic modification</td><td>PC2 NLRD 2.1 (i)</td></tr>
<tr><td>Drug resistance genes or other nucleic acid that could impair practical treatment of any disease or abnormality caused by the viral vector</td><td>DNIR 3.1 (n)</td><td>DNIR 3.1 (o)</td><td>DNIR 3.1 (n)</td><td>DNIR 3.1 (o)</td></tr>
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