[redacted]

From: [redacted] on behalf of OGTR CDES
Sent: Wednesday, 15 April 2015 12:07
To: [redacted]
Subject: RE: Response to query regarding use of siRNA, oligos and CRISPR-CAS genome editing [SEC=UNCLASSIFIED]

Dear [redacted]

[redacted]

As [redacted] mentioned that CRISPR-CAS relatively new technology and the subject of ongoing discussion as to the extent to which it's captured by the current regulatory scheme.

After looking at the information provided, I would agree with the IBC that *in vitro* dealings with lentiviral system proposed to be used would meet the criteria as described under Schedule 2.1(l) as it currently stands.

However, *in vivo* dealings with the lentiviral system may or may not meet the criteria as described under Schedule 2.1(l), depending upon the characteristics of CAS9 gene encoded by the lentiviral system.

[redacted]

I hope this helps

Kind Regards

[redacted]

[redacted] | Contained Dealings Evaluation Section | Phone [redacted]
Office of the Gene Technology Regulator | Street address: Level 1, 15 National Crt, Barton ACT 2600 | Postal address: MDP 54 - GPO Box 9848, Canberra ACT 2601 | Freecall 1800 181 030 | Fax (02) 62714202 | http://www.ogtr.gov.au

---

From: [redacted]
Sent: Friday, 13 March 2015 11:21 AM
To: OGTR Applications
Cc: [redacted]
Subject: FW: Response to query regarding use of [redacted] oligos and CRISPR-CAS genome editing [SEC=UNCLASSIFIED]

Dear OGTR,

In relation to your response below I would like to ask for advice regarding the application attached.

As I understand, introducing CRISPR-CAS into cells would fall under the exempt schedule. However, the researcher is aiming to use CRISPR technology to generate non-replicative recombinant lentivirus, so we would classify this as PC2 dealing.

Our questions are

a) Could you please confirm that the CRISPR/Lenti vector system is regulated under Schedule 2.1.(l)
b) Could you please let us know whether the dealings with the different delivery systems should be recorded and reported separately?

Thanks and Kind Regards
[redacted]

[redacted]
SA Pathology
[redacted]

http://www.sapathology.sa.gov.au/

Research Directorate
SA Pathology
PO Box 14 Rundle Mall, Adelaide, SA, 5000

For our patients and our population

From: [redacted]@health.gov.au] **On Behalf Of** OGTR CDES
Sent: Tuesday, 27 January 2015 1:37 PM
To: [redacted]
Cc: [redacted]
Subject: Response to query regarding use of [redacted] oligos and CRISPR-CAS genome editing [SEC=UNCLASSIFIED]

Dear [redacted]

In response to your query last week, I can offer the following advice.

[redacted] **oligos introduced into:**

Cell lines
[redacted] oligos are considered non-vector systems in Schedule 2 Part 2 of the Regulations. Thus, this would be an exempt dealing under Schedule 2 item 4 of the Regulations, as long as all the criteria listed are met. Once the [redacted] oligo is no longer present in the cells, provided it has not caused any persistent changes (e.g. through changes to DNA methylation), the cells would no longer be considered GMOs.

Animals (non-germline cells)
As animals are not exempt hosts, our view is that the actual dealing (introducing the [redacted]) would be an NLRD under Schedule 2 Part 2.1 (c). Once the [redacted] is no longer present in the animal, provided germline cells have not been modified, the animal itself would not be considered a GMO (Schedule 1 Item 2). However, should the [redacted] have caused a genetic change that persists in the (non-germline) cells it entered, further work with the animal could be considered as an exempt dealing under Schedule 2 Item 3.

Single cell embryos
Early non-human embryos, cultured *in vitro*, are an exempt host, so the advice given for tissue culture cells would apply. If they are used to produce animals, and the [redacted] oligo causes a heritable change in the cells, then dealings with the resulting animals would be as for other transgenic animals i.e. PC1 NLRD under 1.1(c) or PC2 NLRD under 2.1(aa).

CRISPR-CAS-mediated genome editing technology

This is a relatively new technology and the subject of ongoing discussion as to the extent to which it's captured by the current regulatory scheme. OGTR can provide advice on specific examples on a case-by-case basis, but this is a lengthy process. At this stage, it may be prudent to assume that work with CRISPR-CAS does fall within the scheme. Under the current regulations, CRISPR-CAS technology could be considered as involving the introduction of a non-vector system and/or non-conjugative plasmid (crRNA and Cas9 RNA/expression plasmid). Classification of dealings and resulting organisms would then be similar to the advice given in relation to [redacted] oligos, save that changes to the genome would be heritable.

The Gene Technology Regulations are periodically reviewed in response to input from regulated organisations as well as operational experience within the OGTR. The OGTR continually monitors advances in gene technology and how they should best be captured by the regulatory framework. These considerations feed into the regular review of the Regulations.

We encourage your organisation to make a submission to the Gene Technology Regulator regarding CRISPR/CAS-mediated genome engineering so that it can be considered when the Regulations are next reviewed. While a commencement date for the next review has not been set, submissions can be made at any time.

Please don't hesitate to ask if you need any further information regarding this query.

Kind regards,

[redacted]

[redacted]
Contained Dealings Evaluation Section
Office of the Gene Technology Regulator
Ph: [redacted] | Fax: 02 6271 4202
Email [redacted]