Environmental Protection Agency
An Ghníomhaireacht um Chaomhnú Comhshaoil

Headquarters
PO Box 3000
Johnstown Castle Estate
County Wexford
Ireland

Consent to a deliberate release of a GMO into the environment for purposes other than for placing on the market

GMO Register Number:	**G0726-01**
SNIF Reference Number:	**B/IE/20/01**
GMO Notifier:	**Wellcome-HRB Clinical Research Facility** **St James's Hospital** **James's Street** **Dublin 8** **Children's Hospital Ireland** **Temple Street** **Rotunda** **Dublin 1**
Location of the Deliberate Release activity:	**Wellcome-HRB Clinical Research Facility** **St James's Hospital** **James's Street** **Dublin 8**

Genetically Modified Organisms (Deliberate Release) Regulations, 2003
(S.I. No. 500 of 2003)

Decision of the Agency, under Artide 18(5)(a) of the Genetically Modified Organisms (Deliberate Release) Regulations, 2003 (S.I. No. 500 of 2003).

Consent to a deliberate release of a GMO into the environment for purposes other than for placing on the market

Register of Genetically Modified Organisms (GMOs) Users in Ireland: G0726-01

SNIF Reference No: B/IE/20/01

The Agency in exercise of the powers conferred on it by the Genetically Modified Organisms (Deliberate Release) Regulations, 2003 (S.I. No. 500 of 2003) hereby grants consent to:

Wellcome-HRB Clinical Research Facility
St James's Hospital
James's Street
Dublin 8

And

Children's Hospital Ireland
Temple Street
Rotunda
Dublin 1

to carry out the following activity for purposes other than for placing on the market:
The administration of AVXS-101 gene therapy treatment to paediatric patients under 2 years of age, diagnosed with spinal muscular atrophy (SMA), caused by mutations in the survival motor neuron 1 (SMN1) gene

The aforementioned activity will be preformed in the following location:
Wellcome-HRB Clinical Research Facility
St James's Hospital
James's Street
Dublin 8

The period of release extends from the date of grant of these consent conditions to 31st December 2020.

SEALED by the Seal of the Agency on this the 13 day of March 2020

PRESENT when the seal of the Agency was affixed hereto:

Ray Cullinane

Ray Cullinane
Authorised Person

DECISION

The Agency, in exercise of the powers conferred on it by the Genetically Modified Organisms (Deliberate Release) Regulations, 2003 (S.I. No. 500 of 2003) for the reasons hereinafter set out, grants this consent to:

Wellcome-HRB Clinical Research Facility
St James's Hospital
James's Street
Dublin 8

And

Children's Hospital Ireland
Temple Street
Rotunda
Dublin 1

to carry on the deliberate release into the environment for purposes other than for placing on the market in the following location:

Wellcome-HRB Clinical Research Facility
St James's Hospital
James's Street
Dublin 8

subject to nine conditions and the annexes attached hereto.

REASONS FOR THE DECISION

The Agency is satisfied on the basis of the information provided that, subject to compliance with the conditions of this consent, the notifier will ensure that all appropriate measures are taken to avoid adverse effects on human health and the environment. Furthermore, the Agency believes that, subject to compliance with the conditions of this consent, the risks to human health and the environment from the deliberate release of these GMOs are negligible.

In arriving at its decision, the Agency considered the following aspects:

i. *the patient receiving the treatment insofar as they are part of the general population and the wider environment;*

ii. *the potential risk of the GMOs moving from the patient to the general population and the consequences of such a risk; and*

iii. *potential environmental concerns.*

The Agency did not consider the risks that the treatments might pose for the patient.

In reaching this decision, the Agency has considered the notification and supporting documentation received in respect of the notification and the report of its inspector.

The consent is granted in accordance with Article 18(5)(a) of the Genetically Modified Organisms (Deliberate Release) Regulations, 2003 (S.I. No. 500 of 2003).

INTERPRETATION

Agency	The Environmental Protection Agency (EPA).
Competent Authority	The Environmental Protection Agency is the Competent Authority for the purposes of the GMO (Deliberate Release) Regulations, 2003 (S.I. No. 500 of 2003).
Consent	Consent issued in accordance with Article 18(5) of the GMO (Deliberate Release) Regulations, 2003, (S.I. No. 500 of 2003)
Deliberate Release	Means any intentional introduction into the environment of a genetically modified organism or a combination of genetically modified organisms for which no specific containment measures are used to limit their contact with, and to provide a high level of safety for, the general population and the environment. This deliberate release relates to the administration of a gene therapy product (AVXS-101) to paediatric patients under two years of age diagnosed with Spinal Muscular Atrophy (SMA) under a managed access programme.
Directive	Means Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC.
Environmental Risk Assessment	Means an evaluation, carried out in accordance with the Second Schedule of the GMO (Deliberate Release) Regulations S.I. No 500 of 2003, of risks to human health or the environment, whether direct or indirect, immediate or delayed, which the deliberate release or the placing on the market of a genetically modified organism may pose.
Facility	Facility in this instance relates to the Wellcome-HRB Clinical Research Facility within St James's Hospital where the deliberate release activity will be carried out.
GMO	Genetically Modified Organism means an organism, other than a human being, in which the genetic material has been altered in a way that does not

	occur naturally by mating or natural recombination or by a combination of both. For the purposes of this deliberate release, the GMO is AVXS-101 - a recombinant adeno-associated virus serotype 9 (AAV9) capsid shell containing the cDNA of the human Survival Motor Neuron (SMN) gene under the control of the cytomegalovirus (CMV) enhancer/chicken-β-actin-hybrid promoter (CB) as well as two AAV inverted terminal repeats (ITR) from the AAV serotype 2 (AAV2).
GMO Register	A register of GMO users in Ireland, which is available for viewing on the Agency's webpage and at Agency Headquarters. Information provided in the register includes details of the notifier, the location and date or dates of the deliberate release, a description and intended uses of the GMO involved and the purpose of the deliberate release activity.
GMO Regulations	Genetically Modified Organisms (Deliberate Release) Regulations, 2003 (S.I. 500 of 2003).
Micro-organism	Micro-organism means any microbiological entity, cellular or non-cellular, capable of replication or of transferring genetic material, including viruses, viroids, and animal and plant cells in culture.
Notification	A notification means the submission of required information to the competent authority.
Notifier	Means any legal or natural person submitting a notification or, where the context so requires, any legal or natural person responsible for a deliberate release or for a placing on the market, or for meeting any other requirement of the Genetically Modified Organisms (Deliberate Release) Regulations, 2003 in relation to a deliberate release or a placing on the market.
Obligation	A person who carries out a deliberate release or placing on the market shall ensure that all appropriate measures are taken to avoid adverse effects on human health or the environment arising from the deliberate release or placing on the market.
Organism	Means any multicellular, unicellular, subcellular or acellular entity capable of replication or of transferring genetic material whether by natural or artificial processes or such other matter as may be prescribed by the Minister (Minister for Communications, Climate Action & Environment).

SMA	Spinal Muscular Atrophy.
SOPs	Standard Operating Procedures.

Consent Conditions for GMO Register Entry No: G0726-01

Condition 1 Scope

1.1 This consent is for the purposes of compliance with the Genetically Modified Organisms (Deliberate Release) Regulations, 2003 (S.I. No. 500 of 2003) only, in relation to the carrying out of a deliberate release activity as specified in Condition 2.

1.2 Nothing in this consent shall be construed as negating the statutory obligations or requirements of the notifier:

- Wellcome-HRB Clinical Research Facility, St James's Hospital, James's Street, Dublin 8; and,
- Children's Health Ireland, Temple Street Hospital, Temple Street, Dublin 1

under any other enactments or regulations.

1.3 No modifications to the deliberate release, as described in the notification and supporting information submitted to the Agency, shall take place without the prior approval of the Agency.

Reason:	**To clarify the scope of the consent**

Condition 2 Location of the Deliberate Release

2.1 This consent is for the purposes of administering AVXS-101 gene therapy treatment to paediatric patients under 2 years of age diagnosed with SMA at the following location:

Wellcome-HRB Clinical Research Facility
St James's Hospital
James's Street
Dublin 8

Reason:	**To clarify the location of the Deliberate Release**

Condition 3 Duration of the Deliberate Release

3.1 This consent shall extend from the date of grant of these consent conditions to 31st December 2020. No deliberate release of the GMO shall take place after this date.

Reason:	**To clarify the duration of the Deliberate Release**

Condition 4 Management of the Deliberate Release

4.1 The deliberate release shall be carried out at Wellcome-HRB Clinical Research Facility, St James's Hospital by pharmacological, consultant and nursing staff suitably trained in the handling and manipulation of the GMO.

4.2 The responsibility assigned in Condition 4.1 shall include responsibility for reception, storage, preparation and administration of the GMO. It shall also include responsibility for the inactivation and disposal of all GMO contaminated materials used during the course of the deliberate release.

4.3 Access to the storage area, clean room and isolation room where the GMO will be stored, prepared and administered to the patient, respectively, will be restricted to trained designated staff.

4.4 The notifier shall provide the name and contact details of the person responsible for overseeing this deliberate release activity at Wellcome-HRB Clinical Research Facility, St James's Hospital, James's Street, Dublin 8. These details shall be communicated to the Agency prior to the commencement of the deliberate release. Any change to this designation during the deliberate release shall be notified immediately to the Agency.

4.5 All communications with the Agency in relation to this deliberate release shall be through the person identified to the Agency under Condition 4.4.

4.6 Staff involved in performing specifically assigned tasks shall be:

4.6.1 Made aware of risks relating to the GMO associated with the release;
4.6.2 Made aware of possible routes of exposure to the GMO and the procedures to follow in the event of accidental exposure.

4.7 Prior to the commencement of the deliberate release the necessary facilities for the storage, transport, manipulation and inactivation of the GMO shall be made available at the deliberate release location as stipulated under Condition 2.1.

Reason:	**To make provision for management of the activity on a planned basis having regard to the desirability of ongoing assessment, recording and reporting of matters affecting the environment**

Condition 5 Duty of the notifier to inform the Agency of new information

5.1 If, following the granting of this consent, new information relevant to the deliberate release becomes available, or there is an unintended change to the deliberate release which could have consequences for the risks to human health or the environment, the notifier shall:

5.1.1 Immediately take the necessary measures to protect human health and the environment;
5.1.2 Inform the Agency as soon as the new information becomes available or the unintended change is known;

5.1.3 Inform the Agency as soon as possible of such further measures the notifier has taken or proposes to take in relation to the matters concerned.

5.2 The Agency may, following an evaluation of the matters concerned:

5.2.1 Modify the consent conditions; or,
5.2.2 Suspend or terminate the deliberate release.

5.3 In the event that the Agency suspends the deliberate release further to the evaluation of the new information/unintended change, the deliberate release activity shall not resume until such time as the notifier obtains written consent from the Agency permitting its recommencement.

Reason: To provide and update information on the deliberate release

Condition 6 Containment measures to be used at the Deliberate Release Site

6.1 In order to keep the exposure of humans and the environment to the GMO, to the lowest practicable level and to ensure a high level of safety, the notifier shall apply:

6.1.1 The general principles of Good Microbiological Practice and of Good Occupational Safety and Hygiene (reproduced in *Annex II* attached);
6.1.2 Containment measures 3, 9, 13, 14, 15, 17 and 18, corresponding to the Class of the GMM (containment level 1 measures) as set out in Table IA of the Fourth Schedule of the GMO (Contained Use) Regulations (2001 to 2010), (reproduced in *Annex III* attached).

6.2 Personal Protective Equipment

6.2.1 Staff preparing the GMO for patient administration or administering the GMO to the patient or in attendance for purposes of verification against the deliberate release protocol, will be required to wear suitable protective clothing, including mob cap, gown, double gloves, disposable safety glasses, overshoes and mask and any other protective clothing as may be deemed necessary by the notifier.
6.2.2 Gowns and other protective clothing shall be worn only in the work area and shall be removed and disposed of as biohazard waste after use.

6.3 Storage

6.3.1 The GMO shall be stored separately and securely for not more than 14 days, in a dedicated fridge within the Wellcome-HRB Clinical Research Facility at St James's Hospital, Dublin 8.
6.3.2 Access to the GMO fridge shall be restricted to designated staff.
6.3.3 The notifier shall maintain a record of the dates of receipt of the GMO, batch numbers (if relevant), the volume of GMO received and the date of removal from the fridge for preparation for patient

administration. The volume prepared for patient administration shall also be recorded.

6.4 Transport

6.4.1 The GMO shall be transported within secondary containment (a sealed, leakproof and unbreakable container with appropriate labelling) within the CRF facility to minimise the potential for spillage.
6.4.2 Spill kits shall be made available during transport to contain and clean-up any accidental spill.

6.5 Preparation of the GMO for administration

6.5.1 Preparation of the GMO for patient administration shall take place within a pharmaceutical isolator within a clean room by a trained pharmacist using aseptic techniques.
6.5.2 The isolator shall be decontaminated after use using a virucidal disinfectant that is known to effectively destroy Adeno Associated Virus (AAV). The manufacturer's instructions shall be adhered to.
6.5.3 Spill kits shall be made available during preparation to clean-up any accidental spill.

6.6 Administration of the GMO

6.6.1 Staff responsible for the administration of the GMO shall be familiar with the deliberate release risk assessment as well as with procedures that minimise exposure of the GMO to themselves and to the environment.
6.6.2 The isolation room where GMO administration shall take place shall be decontaminated after use, using virucidal disinfectant and in accordance with local SOPs.
6.6.3 Spill kits shall be made available during administration to clean-up any accidental spill

6.7 Aftercare

6.7.1 The notifier shall prepare a detailed instruction sheet identifying the bodily fluids that are potentially contaminated with vector DNA and how to clean up these fluids and properly dispose of the waste.
6.7.2 These instructions shall be given to the patient families and carers.
6.7.3 The notifier shall discuss the instructions with the parents / carers so that they clearly understand the risks to them and others living in the home or to those who come into close contact with the patient.
6.7.4 Parents / carers shall be directed to adhere to the instructions for a period of 60 days post infusion.
6.7.5 Instructions given to patient families and carers shall include but are not limited to the following:
- the wearing of protective gloves and disposable aprons during nappy changes;
- the adoption of good hygiene practices further to:
  - nappy changes;
  - coming into contact with bodily fluids (urine, saliva).

- Good hand hygiene practices which shall include regular hand washing or the regular use of hand sanitizers.
- The disposal of GMM contaminated gloves, aprons, soiled nappies / wipes in a clearly labelled biohazard bin which shall be stored securely away from other family members, pets or animals.
- The collection of the biohazard bin weekly by waste contractor and transport to the site of waste inactivation in accordance with condition 8.

6.8 Standard Operating Procedures (SOPs)

6.8.1 Prior to the date of commencement of the deliberate release, the notifier shall ensure that the following SOPs relating to the performance of the GMO deliberate release activity within the facility, are implemented:

- Measures for limiting access to the facility;
- Work apparel, personal protective equipment;
- Receipt of the GMO;
- Secure storage of the GMO;
- Transport, movement and handling of the GMO;
- Preparation of the GMO for patient administration;
- Administration of the GMO to the patient;
- Treatment of GMO spillages with disinfectants;
- Cleaning and disinfection of non-disposable equipment;
- Validation, servicing, control and maintenance of containment equipment;
- Storage and inactivation of GMO contaminated waste;
- Maintenance of records relating to the receipt and storage of the GMO, staff training and the removal of GMO waste for inactivation;
- Worker protection measures to be taken during the release.

6.8.2 SOPs shall be made available to all relevant staff prior to commencement of the deliberate release and to the Agency upon request.

6.8.3 SOPs shall be reviewed annually.

Reason:	**To ensure proper management of the deliberate release and to avoid adverse effects on human health and the environment arising from the deliberate release**

Condition 7 Worker Protection Measures to be taken during the deliberate release

7.1 All persons with access to the work area where the deliberate release shall be carried out shall be informed about the deliberate release and the use of the GMO.

7.2 All staff involved in the deliberate release activity shall be appropriately trained according to GMO risk assessments and local standard operating

procedures (SOPs) as set out under condition 6.8 prior to commencement of the deliberate release.

7.3 The notifier shall implement worker protection measures during the deliberate release. These measures shall apply to all staff involved in the execution of the deliberate release and shall include pprocedures to follow in the event of accidental exposure.

Reason:	**To comply with the legislation and to avoid adverse effects on human health and the environment**

Condition 8 Waste Management

8.1 Disposable materials contaminated with the GMO shall be disposed of into a clearly labelled, biohazard bin while awaiting collection by an authorised waste contractor. Waste storage containers shall display biohazard signs.

8.2 GMO contaminated sharps waste including but not limited to contaminated vials, syringe, infusion set and tubing and patient cannula shall be disposed of into sharps containers. Sharps containers shall in turn be placed in biohazard bins.

8.3 GMO contaminated waste placed in biohazard bins and destined for off-site treatment shall be stored securely prior to collection, to prevent the risk of human or environmental exposure to the waste. Access to the waste storage facility shall be restricted to authorised persons.

8.4 All GMO contaminated waste shall be inactivated before disposal.

8.5 GMO contaminated waste shall be collected and stored at an approved waste facility, licensed under the GMO (Contained Use) Regulations, (2001-2010), while awaiting transfer to an inactivation facility.

8.6 All GMO contaminated waste shall be transported from the site of the activity to the site of inactivation by a contractor authorised in accordance with the provisions of the appropriate National and European legislation and protocols.

8.7 Spill kits and virucidal disinfectants shall be available for immediate use in the event of a spillage.

8.8 GMO contaminated waste generated in the home shall be disposed of in clearly labelled, biohazard bins. These bins shall be collected weekly by an authorised waste contractor and stored at an approved waste facility, licensed under the GMO (Contained Use) Regulations, (2001-2010), while awaiting transfer to an inactivation facility. All such waste shall be transported from the site of the activity to the waste storage facility and on to the inactivation facility by a contractor authorised in accordance with the provisions of the appropriate National and European legislation and protocols.

8.9 Records of GMO waste inactivation shall be retained by the notifier for inspection by the EPA on request. Such records shall also be retained in respect of the inactivation of home generated GM waste.

Reason:	**To ensure proper management and destruction of GMO waste so as to avoid adverse effects on human health and the environment**

Condition 9 Record Keeping and Reporting to the Agency

9.1 Record keeping and reporting to the Agency shall be in accordance with Annex I.

9.2 The notifier shall inform the Agency of the date of the first deliberate release and the date of the final deliberate release.

9.3 Reports to the Agency on the results of the deliberate release:

9.3.1 The notifier shall submit a report to the Agency, in the format set out under Commission Decision 2003/701/EC[1], (adapted for the release of a human medicinal product) on or before the 31 March 2021.

9.4 All records/reports (including GMO inactivation records) shall be retained by the notifier at the Clinical Research Facility, St James's Hospital for a period of 12 months following completion of the deliberate release. Prior to commencement of the deliberate release, the notifier shall inform the EPA of the position of the person in Wellcome-HRB Clinical Research Facility, St James's Hospital with responsibility for these records/reports.

9.5 On completion of the deliberate release, the notifier shall notify the Agency in writing. The notifier shall verify in writing that no GM material relating to this deliberate release is stored in the Wellcome-HRB Clinical Research Facility St James's Hospital.

9.6 Training records signed by all staff in receipt of training relating to the GMO deliberate release activity, shall be approved and maintained by the notifier. These records shall be made available to the Agency on request.

Reason:	**To maintain written records of the deliberate release and make provision for the reporting to the Agency of any impacts of the completed deliberate release and associated risks**

[1] Commission Decision of 29 September 2003 establishing pursuant to Directive 2001/18/EC of the European Parliament and of the Council a format for presenting the results of the deliberate release into the environment of genetically modified higher plants for purposes other than placing on the market (*notified under document under C(2003) 3405*) (2003/701/EC)

Annex I

SCHEDULE OF REPORTING / MAKING INFORMATION AVAILABLE

Deadline	**Information to be submitted to the EPA**	**Information to be made available to deliberate release staff**
To be provided prior to commencement of deliberate release	Notifier Provide the name and contact details of a person with responsibility for overseeing the performance of this deliberate release activity at Wellcome-HRB Clinical Research Facility, St James's Hospital, James's Street, Dublin 8 (Condition 4.4). Any change to this designation shall be notified to the Agency immediately, (Condition 4.4)	Notifier shall make available to staff: • SOPs set out under Condition 6.8
	Notifier Date of deliberate release commencement (Condition 9.2)	
	Notifier Implementation of SOPs set out under Condition 6.8	Notifier shall make available to staff: • Risks relating to the GMO • Possible routes of exposure to the GMO • Procedures to follow in the event of accidental exposure
	Notifier The position of the person responsible for reports/ records (Condition 9.4)	
To be made available to the Agency on request.	GMO waste inactivation records (Condition 8.9)	
	Training records (Condition 9.6)	
To be provided to the Agency on completion of the deliberate release	Notifier • Date of deliberate release completion (Condition 9.2) • Report in the format set out under Commission Decision 2003/701/EC (Condition 9.3)	

Annex II

Principles of good microbiological practice and good occupational safety and hygiene practice shall include:

(i) keeping the workplace and environmental exposure to any genetically modified micro-organism to the lowest practicable level;

(ii) exercising engineering control measures at source and where necessary supplementing these with appropriate personal protective clothing and equipment;

(iii) testing and maintaining control measures and equipment;

(iv) testing where necessary for the presence of viable process organisms outside the primary physical containment;

(v) providing appropriate training of personnel;

(vi) establishing biological safety committees or subcommittees where required;

(vii) formulating and implementing local codes of practice for the safety of personnel where required;

(viii) where appropriate displaying biohazard signs;

(ix) providing washing and decontamination facilities for personnel;

(x) keeping adequate records;

(xi) prohibiting eating, drinking, smoking, applying cosmetics or the storing of food for human consumption in the work area;

(xii) prohibiting mouth pipetting;

(xiii) where appropriate, providing written standard operating procedures to ensure safety;

(xiv) having effective disinfectants and specified disinfection procedures available in the case of spillage of genetically modified micro-organisms and;

(xv) where appropriate, providing safe storage for contaminated laboratory equipment and materials.

Annex III

Table IA

Containment measures for contained use of genetically modified micro-organisms in a laboratory

Measures		**Containment levels**			
		1	2	3	4
1	Laboratory Suite: Isolation	Not required	Not required	Required	Required
2	Laboratory: sealable for fumigation	Not required	Not required	Required	Required
Equipment					
3	Surfaces resistant to water, acids, alkalis, solvents, disinfectants, decontamination agents and easy to clean	**Required for bench**	Required for bench	Required for bench and floor	Required for bench, floor, ceiling and walls
4	Entry to laboratory via airlock	Not required	Not required	Optional	Required
5	Negative pressure relative to the pressure of the immediate environment	Not required	Not required	Required	Required
6	Extract and input air from the laboratory should be HEPA-filtered	Not required	Not required	Required	Required for input and extract air
7	Microbiological safety cabinet	Not required	Optional	Required	Required
8	Autoclave	On site	In the building	En suite	Double-ended autoclave in laboratory
System of work					
9	Restricted access	**REQUIRED**	Required	Required	Required
10	Biohazard sign on the door	Not required	Required	Required	Required
11	Specific measures to control aerosol dissemination	Not required	Required to minimise	Required to prevent	Required to prevent
12	Shower	Not required	Not required	Optional	Required
13	Protective Clothing	**Suitable protective clothing**	Suitable protective clothing; footwear optional	Suitable protective clothing and footwear	Complete change of clothing and footwear before

					entry and exit
14	Gloves	**REQUIRED**	Optional	Required	Required
15	Efficient vector control (e.g. for rodents and insects)	**REQUIRED**	Required	Required	Required
Measures		**Containment levels**			
		1	2	3	4
Waste					
16	Inactivation of genetically modified micro-organisms in effluent from hand-washing sinks or drains and showers and similar effluents	Not required	Not required	Optional	Required
17	Inactivation of genetically modified micro-organisms in contaminated material and waste	**REQUIRED**	Required	Required	Required
Other Measures					
18	Laboratory to contain its own equipment	**REQUIRED**	Not required	Optional	Optional
19	Observation window or alternative to enable occupants to be seen	Optional	Optional	Optional	Required

For the purpose of this Table:

(1) In measure 1, "*isolation*" means that the laboratory is separated from other areas in the same building or is in a separate building

(2) In measure 4, "*airlock*" means that the entry must be made through a chamber isolated from the laboratory. The clean side of the airlock must be separated from the restricted side by changing or showering facilities, or by interlocking doors.

(3) In measure 5, "*negative pressure relative to the pressure of the immediate environment*" is only required for a class 3 contained use where airborne transmission can occur.

(4) "*HEPA*" means high efficiency particulate air.

(5) In measure 6, where viruses which are not capable of being retained by HEPA filters are used in class 4 contained use, extra requirements shall be provided for extract air.

(6) In measure 8, "en suite" means that where the autoclave is located outside the laboratory in which the contained use is being carried out but within the laboratory suite, validated procedures shall be in place to ensure the safe transfer of material into the autoclave and to provide a level of protection equivalent to that which would be achieved if the autoclave were in the laboratory.

Sealed by the seal of the Agency on this the 13 day of March 2020.

PRESENT when the seal of the Agency was affixed hereto:

Ray Cullinane

Ray Cullinane
Authorised Person