

Summary of representative risk management measures (RMMs) and operational conditions (OCs)

Public Version

Legal name of applicant: MeiraGTX UK II Limited

Submitted by: MeiraGTX UK II Limited

Substance: 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated [covering well-defined substances and UVCB substances, polymers and homologues]

Use title: Use of 4-tert-OPnEO as a manufacturing aid in the production of gene therapies

Use number: 1

Declaration

The Applicant is aware of the fact that evidence might be requested by the Health and Safety Executive to support information provided in this document.

Also, we request that the information blanked out in the "public version" of the Risk Management Measures and Operational Conditions is not disclosed. We hereby declare that, to the best of our knowledge as of today (15th January 2021) the information is not publicly available, and in accordance with the due measures of protection that we have implemented, a member of the public should not be able to obtain access to this information without our consent or that of the third party whose commercial interests are at stake.

Signature:



Date, Place:

18th Jan 2021

London

OK

ES1: Use of 4-tert-OPnEO as a manufacturing aid in the production of gene therapies

ECS and WCS	Task (ERC/spERC or PROC)	Annual amount per site (tonnes/year)	Technical RMMs, including: *Containment, *Ventilation (general, LEV ...) *customized technical installation, etc	Organisational RMMs, including: *Duration and Frequency of exposure *OSH management system *Supervision *Monitoring arrangements *Training, etc	PPE (characteristics)	Effectiveness of wastewater and waste air treatment (for ERC)	Release factors: water, air and soil (for ERC)	Detailed info. in CSR (section)
ECS-1	ERC 4	c				<p>No wastewater treatment onsite.</p> <p>The unused 4-tert-OPnEO, b and the apparatus used is removed off-site by an external contractor for hazardous waste incineration.</p>	<p>Water: c Minimal release of tert-OPnEO (approx. [c]) to wastewater per batch. Maximum of a batches per day.</p> <p>Air: 0% No releases expected as the substance is non-volatile and takes place indoors.</p> <p>Soil: 0%</p>	Section 1.3

								There is no direct release since the process takes place indoors in controlled areas.	
WCS 1.1	PROC 0 Receipt and Storage of 4-tert-OPnEO		4-tert-OPnEO is received in a glass bottles which are stored in a chemical cabinet. General ventilation	When requested, the bottle is cleaned as per the standard operating procedure (SOP) and sent in a goods lift to the ground floor production facility. Material quantities, status and locations are controlled using a Quality System, and employees are trained in company procedures on cGMP and SOPs.	NA	NA	NA	NA	NA
WCS 1.2	PROC 8b Transfer of 4-tert-OPnEO into a b		4-tert-OPnEO is decanted into b. HVAC system	<15 minutes exposure Less than a, b a day All staff trained in standard operating procedures (SOPs) for production.	Gloves Safety glasses Cleanroom gowns	NA	NA	NA	NA
WCS 1.3	PROC 3		The excess 4-tert-OPnEO contained	<15 minutes exposure	Gloves Safety glasses	NA	NA	NA	NA

	Excess 4-tert-OPnEO sent for disposal.	within the glass bottle is transferred by the materials transfer hatch for disposal. Potential for exposure upon closure of bottle. HVAC system	Less than a,b a day All staff trained in standard operating procedures (SOPs) for production.	Cleanroom gowns			
WCS 1.4	PROC 8b Transfer from b to bioprocessing bag	The transfer occurs using b b . Bag is then sealed. Possibility of exposure during sealing of the bag. HVAC system	<15 minutes exposure Less than a,b a day All staff trained in standard operating procedures (SOPs) for production.	Gloves Safety glasses Cleanroom gowns	NA	NA	NA
WCS 1.5	PROC 3 Storage of bioprocessing bag in fridge	Contained within sealed bioprocessing bag. No exposure expected. HVAC system	<15 minutes exposure Less than a,b a day All staff trained in standard operating procedures (SOPs) for production	NA	NA	NA	NA
WCS 1.6	PROC 8b Contents of bioprocessing	b is sent to bioprocessing (BVP) room via the materials transfer	<15 minutes exposure	Gloves Safety glasses Cleanroom gowns	NA	NA	NA

	bag transferred to bioreactor		hatch and transferred to two bioreactors. HVAC system	Less than twice a day All staff trained in standard operating procedures (SOPs) for production				
WCS 1.7	PROC 9 Sampling of bioreactor		Collection of a sample via a sampling port on the bioreactor. A sample is pumped out at the desired volume. HVAC system	<15 minutes exposure Up to 100 samples per batch All staff trained in standard operating procedures (SOPs) for production	Gloves Safety glasses Cleanroom gowns	NA	NA	NA
WCS 1.8	PROC 8b Transfer of contents from the bioreactor to the bioprocessing bag			<15 minutes exposure Less than a day All staff trained in standard operating procedures (SOPs) for production	Gloves Safety glasses Cleanroom gowns	NA	NA	NA
WCS 1.9	PROC 9 Sampling of lysate		Sample is contained within sealed container. Sample is sent to Quality Control and tested. HVAC system	<15 minutes exposure Up to 100 samples per batch All staff trained in standard operating procedures (SOPs) for production	Gloves Safety glasses Cleanroom gowns	NA	NA	NA

WCS 1.10	PROC 3 PROC 8b Purification of lysate b		4-tert-OPnEO contained within b equipment. Once eluted, the material is collected into a bioprocessing bag and sealed. HVAC system	<15 minutes exposure Less than a,b a day All staff trained in standard operating procedures (SOPs) for production	Gloves Safety glasses Cleanroom gowns	NA	NA	NA
WCS 1.11	PROC 15 Laboratory analysis of final product		Sample is contained within sealed container. Sample is sent to Quality Control and tested. HVAC system	<15 minutes exposure Up to 100 samples per batch All staff trained in standard operating procedures (SOPs) for production	Gloves Safety glasses Cleanroom gowns	NA	NA	NA

Abbreviations: WCS=Worker contributing scenario, ECS=Environmental Contributing Scenario, * ERC=Environmental Release Category (or spERC if available), PROC= Process category, LEV=Local Exhaust Ventilation, PPE=Personal Protective Equipment

