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MSD

21st July 2021

Ref. IE Licence No. P0011-06

Subject: **Notification of new product MK-8591QM introduction in the Pharmaceutical Operations Facility at the MSD Ireland (Ballydine) plant**

Dear Ms. Doyle,

As per condition 1.4 of our licence, please find attached information in support of the planned product introduction of MK-8591QM tableting, due to commence production from September 2021 in the Pharmaceutical Operations Facility at the MSD Ireland (Ballydine) plant.

The MK-8591QM process is similar to the previously approved MK-8591A process, and as a tablet containing the active ingredient MK-8591 Islatravir API, developed for the treatment of human immunodeficiency virus (HIV).

MSD Ireland (Ballydine) plan to complete developmental production campaigns of the new product MK-8591QM during 2021-2022, before going into commercial supply production from 2023 in the Pharmaceutical Operations Facility.

The manufacturing will involve the use of existing equipment trains without modification or without creation of any new emission points. Existing site abatement and waste management facilities are adequately sized to treat all API and excipient waste.

Attached for your reference are details of the API, excipients and waste streams used or generated on the site during the proposed tableting of MK-8591QM.

We trust that this proposal meets with your approval.

Yours sincerely

David O'Gorman
Sr Specialist, Safety & Environment

Public disclosed

1.0 INTRODUCTION.

The Pharmaceutical Operations Plant is in operation since April 2010. The new process MK-8591QM involves using some of the existing process trains without modification. The equipment modules are dispensing, sieving, blending, roller compaction and tablet compression.

The production of these new tablets does not involve the introduction of any new API or excipients to the Pharm Ops facility. The MK-8591QM product is for the treatment of HIV.

Any waste API which may be generated during processing will be drummed and disposed of as per site procedures by offsite incineration. Sufficient controls and treatment options exist to treat all solid waste streams from the Pharm Ops facility.

The Pharmaceutical Operations facility does not use any solvents in processing.

2.0 PROCESS DETAILS.

The existing MK-8591 Islatravir API is supplied from one of the bulk API synthesis facilities onsite at MSD Ireland (Ballydine).

For the production of MK-8591QM tablets, the MK-8591 Islatravir API along with the excipients will be sieved directly into an IBC and from there into the Blender for diffusion (tumble) blending. The lubricant, magnesium stearate will be added to the IBC and the mixture further blended. The lubricated mixture will then be passed through a roller compaction unit to granulate the blend. The compacted material will have more magnesium stearate added and then blended again. During the compression step, the MK-8591QM granulate will be compressed into monolayer tablets on a rotary tablet press. The tablets will be placed into containers for storage, shipping, and packaging operations at an external facility.

It is planned to commence MK-8591QM development batches during September 2021 and 2022, and then commercial supply production from 2023 and over subsequent years.

The projected peak total annual tonnage of raw materials used in the production of MK-8591QM tablets will be less than 30 tonnes.

Annual Materials Utilised and their Maximum Quantities

Raw Material	Total Quantity tonnes
MK-8591 Islatravir API	< 10 tonnes
Microcrystalline Cellulose	< 10 tonnes
Lactose Hydrate Fast Flow	< 10 tonnes
Colloidal Silicon Dioxide	< 0.2 tonnes
Croscarmellose Sodium Acdisol	< 1 tonnes
Magnesium Stearate Hyqual	< 0.2 tonnes
** No new materials present not advised in previous new process submissions*	

3.0 OFF-GAS TREATMENT.

There are no volatile components in the manufacture of MK-8591QM tablets.

Atmospheric abatement involves the utilisation of dust collectors and HEPA filters. All emissions are minor in nature and utilise designated existing emission points.

4.0 ODOUR POTENTIAL.

None.

5.0 WASTE STREAM TREATMENT.

Any waste API, intermediate, excipients and tablets which may be generated during production activities will be collected, drummed, and disposed of by offsite incineration.

IPA may be used for final clean/drying of equipment. Its use will be limited to a 1 litre trigger bottle. Amounts going to drain will be minimal and will be treated by the onsite WWTP.

All IE licence parameters for the WWTP outfall will be met.

DRUMMED / PACKAGED WASTE DISPOSAL.

Sufficient approved off-site incineration facilities, equipped with heat recovery, are available to treat solid wastes from the proposed MK-8591QM process.

Plant waste management systems will ensure the proper identification, classification, labelling of solids waste, raw materials, and laboratory samples.

6.0 SDS's.

SDS's are retained on file at MSD Ireland (Ballydine).

There are no new materials introduced to the MSD Ballydine site for the MK-8591QM tableting process.

All the excipients in this process are already in use in other process steps.