CHEMICAL SAFETY REPORT

PUBLIC

Legal name of applicant:	Becton, Dickinson U.K. Limited
Submitted by:	Becton, Dickinson U.K. Limited
Substance:	2-(2*H*-benzotriazol-2-yl)-4,6-ditertpentylphenol (EC No: 247-384-8, CAS No: 25973-55-1), known alternatively as UV-328
Use title:	Use of an imported polymer containing 2-(2H-benzotriazol-2-yl)-4,6-ditertpentylphenol as an additive for UV stabilisation in the manufacturing of a mechanical separator component for blood collection tubes in Becton, Dickinson U.K. Limited's plant in Plymouth.
Use number:	1

CONTENTS

TABLES

FIGURES

LIST OF ABBREVIATIONS

Abbreviation	Definition
AfA	Application for Authorisation
CAS	Chemical Abstract Service
CS	Contributing Scenario
CSR	Chemical Safety Report
DNEL	Derived No Effect Level
EC	European Commission
ECHA	European Chemicals Agency
EHS	Environmental, Health and Safety
ERC	Environmental Release Category
ES	Exposure Scenario
EU	European Union
HvE	Humans via Environment
IPA	Isopropyl Alcohol
LCS	Life Cycle Stage
PBT	Persistent, Bioaccumulative and Toxic
PNEC	Predicted No-Effect Concentration
PC	Product Category
PEClocal	Local Predicted Environmental Concentration
PP	Polypropylene
PPE	Personal Protective Equipment
PROC	Process Category
RAC	Committee for Risk Assessment
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
RMM	Risk management measures
SOP	Standard Operating Procedure
STOT-RE	Specific Target Organ Toxicity-Repeated Exposure
SU	Sector of Use
SQA	Software Quality Assurance
TPE	Thermoplastic elastomer
UK	United Kingdom
UV	Ultraviolet
vPvB	very Persistent, very Bioaccumulative
WCS	Worker Contributing Scenario

DECLARATION

We, Becton, Dickinson U.K. Limited, are aware of the fact that further evidence might be requested by HSE to support the information provided in this document.

Also, we request that the information blanked out in the "public version" of the Chemical Safety Report is not disclosed. We hereby declare that, to the best of our knowledge as of today (20 June 2022) 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 any third party whose commercial interests are at stake.

Daniel Hopkin

Director – Becton, Dickinson U.K. Limited 20 June 2022, Winnersh, UK

Part A

1 SUMMARY OF RISK MANAGEMENT MEASURES

Becton, Dickinson U.K. Limited imports UV-328 incorporated in thermoplastic elastomer (TPE) resin.

UV-328 exhibits environmental (Aquatic Chronic 4, H413) and chronic health hazards (STOT Rep. Exp. 2, H373) and fulfils the criteria for being persistent, bioaccumulative and toxic (PBT) and very persistent and very bioaccumulative (vPvB) according to UK REACH (Registration, Evaluation, Authorisation and restriction of Chemicals) Annex XIII.

The use of UV-328 as an additive for Ultraviolet (UV) stabilization in TPE in an injection moulding system to manufacture mechanical separator components for blood collection tubes used by hospitals and medical professionals has been assessed in part B of this chemical safety report. A summary of risk management measures to control environmental emissions and worker exposure is provided below in the "Succinct Summary".

Table A-1 Succinct Table: Becton, Dickinson U.K. Limited, UV-328 Use 1

ECS and WCS	Task (ERC / PROC)	Annual amount of UV-328 at the site (tonnes/year) (highest amount per year expected within the requested review period)	Technical RMMs, including: *Containment, *Ventilation (general, LEV…) *Customised technical installation, etc.	Organisational RMMs, including: *Duration and Frequency of exposure *OSH management system *Supervision *Monitoring arrangements *Training, etc.	PPE (characteristics)	Other conditions	Effectiveness of waste water and waste air treatment (for ERC)	Release factors: water, air and soil (for ERC)	Detailed information in CSR (chapter)
ECS1	ERC5	[redacted] [0.09-0.16]	Waste treatment: Any solid waste containing UV-328 is sent to an external waste management company (licenced contractor) for disposal as hazardous waste. No liquid waste containing UV-328 occurs. Ventilation: General ventilation: 28,926 m3/h	Operation days: 336 days/year Management system: Advanced EHS management system SOP and training in place	\	Rigorous controlled condition throughout the entire manufacturing process of the mechanical separator. Moulding process in an air-locked area UV328 concentration max. [redacted] [<1]%	\	Air: 0% Water: 0% Soil: 0%	9.1.5 and 9.2.1
ECS2	ERC12	[redacted] [0.09-0.16]	The mechanical separator falls under the definition of an article according to UK REACH. The inclusion of the separator in the blood tube is not a use for AfA purposes						
WCS1	PROC1	[redacted] [0.09-0.16]	General ventilation: 28,926 m3/h	Duration of activity: <= 0.025 h/day (30 min/month) SOP and training in place	None	The TPE resin is sealed in plastic bags in closed octabins	\	\	9.2.3
WCS2	PROC8b	[redacted] [0.09-0.16]	General ventilation: 28,926 m3/h	Duration of activity: 0.066 h/day (20 min/week) SOP and training in place	Chemical resistant gloves	\	\	\	9.2.4

CBI 2

ECS and WCS	Task (ERC / PROC)	Annual amount of UV-328 at the site (tonnes/year) (highest amount per year expected within the requested review period)	Technical RMMs, including: *Containment, *Ventilation (general, LEV…) *Customised technical installation, etc.	Organisational RMMs, including: *Duration and Frequency of exposure *OSH management system *Supervision *Monitoring arrangements *Training, etc.	PPE (characteristics)	Other conditions	Effectiveness of waste water and waste air treatment (for ERC)	Release factors: water, air and soil (for ERC)	Detailed information in CSR (chapter)
WCS3	PROC14	[redacted] [0.09-0.16]	General ventilation: 28,926 m3/h	Duration of activity: <= 8 h/day SOP and training in place	None	Fully enclosed moulding machine	\	\	9.2.5
WCS4	PROC8b	[redacted] [0.09-0.16]	The mechanical separator falls under the definition of an article according to UK REACH. The inclusion of the separator in the blood tube is not a use for AfA purposes						
WCS5	PROC8b	[redacted] [0.09-0.16]	General ventilation: 28,926 m3/h	Duration of activity: <= 0.2 h/day (1 hour/week) SOP and training in place	Chemical resistant gloves	\	\	\	9.2.7
WCS6	PROC19	[redacted] [0.09-0.16]	General ventilation: 28,926 m3/h	Duration of activity: <= 0.4 h/day (2 hours/week) SOP and training in place	Chemical resistant gloves.	\	\	\	9.2.8
WCS7	PROC10	[redacted] [0.09-0.16]	General ventilation: 28,926 m3/h	Duration of activity: <= 1 h/day SOP and training in place	Chemical resistant gloves	\	\	\	9.2.9

CBI 2

2 DECLARATION THAT RISK MANAGEMENT MEASURES ARE IMPLEMENTED

The applicant implements the risk management measures that are discussed in Chapter 9 of Part B of this document.

3 DECLARATION THAT RISK MANAGEMENT MEASURES ARE COMMUNICATED

The risk management measures mentioned in chapter 9 of part B are communicated to all involved employees and any affected third party.

Part B

The present application for authorisation (AfA) is submitted for the use of the Ultraviolet stabilizer UV-328 included as additive to a thermoplastic elastomer (TPE) resin.

Table B-1 Substance identity

EC number	247-384-8
CAS number	25973-55-1
CAS name	Phenol, 2-(2H-benzotriazol-2-yl)-4,6-bis(1,1-dimethylpropyl)-
IUPAC name	2-(2-hydroxy-3;5-di-tert-amyl-phenyl) 2H-benzotriazole
Molecular formula	$C_{22}H_{29}N_3O$
Molecular weight	351.485 g/mol

Composition of the substance

The applicant uses UV-328 with a concentration of [redacted] [<1] wt% of TPE.

CBI 1

9 EXPOSURE ASSESSMENT (AND RELATED RISK CHARACTERISATION)

9.1 Introduction

Phenol, 2-(2H-benzotriazol-2-yl)-4,6-bis(1,1-dimethylpropyl)-has been included into Annex XIV of the EU REACH regulation (list of substances subject to Authorisation) due to its intrinsic properties (persistent, bioaccumulative and toxic (PBT) as well as very persistent and very bioaccumulative (vPvB) substance according to Art. 57(d) and (e) of REACH)) [2]. When UK REACH came into force in the United Kingdom (UK) on 1st January 2021, the UK retained the Authorisation provisions of EU REACH in full.

The substance exhibits environmental (Aquatic Chronic 4, H413) and chronic health hazards (STOT Rep. Exp. 2, H373). According to UK REACH Article 62 (4) (d)[1], the CSR supporting an Application for Authorisation (AfA) needs to cover only those risks arising from the intrinsic properties specified in Annex XIV. Therefore, only the environmental and human health risks related to the classification of UV-328 as PBT / vPvB substance are addressed in this CSR.

Since UV-328 is a non-threshold substance without a well-defined dose-response relationship for its intrinsic properties 'vP' (and 'P') and 'vB' (and 'B'), the present environmental risk assessment does not include any calculation of risk characterisation based on a dose-response curve or a PNEC value thereof. Based on the substances classification for STOT-RE 2 it has also to be considered as toxic ('T'). The available DNELs calculated based on the most sensitive endpoint repeated dose toxicity [2] are used for risk calculations. The aim of this CSR is to demonstrate minimisation of risk, reducing exposure for the use applied for and high awareness of workplace hygiene at the applicant´s facility.

Rigorous controlled conditions to avoid emissions are in place to avoid emissions into the environment. There is no relevant direct exposure path for workers. An indirect exposure path for humans via the environment is not given due to the risk management measures (incineration of all UV-328 waste). Chapter 9 (Exposure Assessment) describes the environmental exposure scenario and it is shown that there is no release of UV-328 to the environment.

9.1.1 Persistent, bioaccumulative and toxic

Persistence
Based on experimental, modelling and monitoring data it can be concluded that UV-328 has a very low degradation potential and long disappearance half-lives (DT_{50}) in soil and sediment. Furthermore, a readily biodegradation test shows that UV-328 has a very low potential for biodegradation (2-8 % after 28 days) [1].

[1] unless already submitted as part of the registration, a chemical safety report in accordance with Annex I covering the risks to human health and/or the environment from the use of the substance(s) arising from the intrinsic properties specified in Annex XIV;

The substance is highly insoluble in water and no hydrolysis is expected, it is not volatile and has a high potential for adsorption. Once released to the environment distribution to soil, sediment and sludge is expected [1, 2].

Bioaccumulation

UV-328 has a log Kow >5 and measured bioconcentration factors show BCF-values >5000 while metabolic transformation rates were low. There is evidence of bioaccumulation of UV-328 in fish, crustaceans, marine mammals and algae [1, 2]. Several monitoring studies show measured concentrations which have been in the order of several hundred ng/g lipid weight [3, 4, 5].

Toxicity

There is evidence that UV-328 is toxic to mammals as it can cause adverse effects upon repeated exposure in specific target organs, primarily the liver and kidneys. Consequently, the Risk Assessment Committee of the European Chemicals Agency concluded that UV-328 meets the criteria for specific target organ toxicity – repeated exposure in sub-category 2 (STOT RE 2) in accordance with the Classification, Labelling and Packaging (CLP) Regulation EC 1272/2008, based on repeated-dose toxicity studies conducted in rats [1, 6].

No evidence regarding the carcinogenicity, genotoxicity, mutagenicity, reproductive or developmental toxicity of UV-328 has been reported, nor are there reports to indicate skin irritation, eye irritation or sensitisation [2] and estrogenic activity [7].

9.1.2 Broad information on use applied for (conditions of use and function)

Key elements of the condition of use and functional requirements:

- Becton, Dickinson U.K. Limited (hereafter referred to as 'Becton Dickinson' or ´the applicant´) imports UV-328 as a component of thermoplastic elastomer (TPE) resin for manufacturing of mechanical separators, which are components of blood collection tubes (Vacutainer® Barricor™ Plasma Blood Collection Tubes (Figure 9-1)). The process of manufacturing mechanical separators is approved by the authorities under ISO 13485:2016.

- TPE is only used by workers at the applicant's facility in Plymouth, UK, in closed processes in accordance with the use conditions set out in this CSR and under Good Manufacturing Practice (GMP). UV-328 is imported incorporated in TPE in a concentration of up to [redacted] [<1] wt%. All waste generated during the use of the substance is collected and disposed of via incineration.

CBI 1

- The final article, the mechanical separator incorporated in Vacutainer®

Barricor™ Plasma Blood Collection Tubes, is exempted from authorisation according to UK REACH Article 56(1)[2]. Consequently, downstream exposure is not applicable for this AfA. The final article has no commercial applications for the general public, as they are only delivered as part of the Vacutainer® Barricor™ Plasma Blood Collection Tubes, to hospitals and medical professionals. At end of life, the mechanical separator and the mechanical separator incorporated in Vacutainer® Barricor™ Plasma Blood Collection Tubes, is disposed of as biohazardous waste via incineration.

- Highly controlled conditions are applied to minimise the potential for exposure to workers and releases to the environment of TPE resin containing UV-328. This includes the unloading operation of TPE resin which is delivered though sealed plastic bags contained in octabins, the storage of the octabins, the loading of TPE resin in the moulding machine which happens into air locked room, and finally the loading of mechanical separators consisting of moulded TPE in the assembly machine for Vacutainer® Barricor™ production.

- The Application for Authorisation covers an annual total amount of [redacted] [100-200] kg of UV-328, corresponding to [redacted] [10,000 – 30,000] kg of TPE resin (considering the worst case scenario of [redacted] [<1]% of UV-328 in TPE resin w/w). CBI 1 & 2

- The requested review period is 4 years.

- *Technical function*: UV-328 is a UV absorber and light stabiliser protecting various surfaces against discoloration and weathering under UV/sunlight. UV-328 absorbs the full spectrum of UV light in a fully reversible and non-destructive process [1].

Technical function of mechanical separator:

- Becton Dickinson Vacutainer® Barricor™ Plasma Blood Collection Tubes (hereafter referred to as the ´blood collection tube´) is a single-use, plastic evacuated tube with a mechanical separator. Used to collect, separate, transport, and process venous blood specimens, the blood collection tube

[2] A manufacturer, importer or downstream user shall not place a substance on the market for a use or use it himself if that substance is included in Annex XIV, unless:

(a) the use(s) of that substance on its own or in a ►M3 mixture ◄ or the incorporation of the substance into an article for which the substance is placed on the market or for which he uses the substance himself has been authorised in accordance with Articles 60 to 64; or

(b) the use(s) of that substance on its own or in a ►M3 mixture ◄ or the incorporation of the substance into an article for which the substance is placed on the market or for which he uses the substance himself has been exempted from the authorisation requirement in Annex XIV itself in accordance with Article 58(2); or

(c) the date referred to in Article 58(1)(c)(i) has not been reached; or

(d) the date referred to in Article 58(1)(c)(i) has been reached and he made an application 18 months before that date but a decision on the application for authorisation has not yet been taken; or

(e) in cases where the substance is placed on the market, authorisation for that use has been granted to his immediate downstream user.

provides a high-quality plasma sample for chemistry determinations and therapeutic drug monitoring, and infectious disease testing in plasma for *in vitro* diagnostic use.

- The mechanical separator is located in the empty blood collection tube at the top of the tube near the septum cap. It consists of two parts made of synthetic polymers, a low density elastomer top and a high density plastic base (Figure 9-1). UV-328 is compounded into the elastomer to ensure stability of the material against degradation caused due to exposure of UV light. This allows mechanical properties that are critical to the blood collection tube's performance to remain acceptable and ensure that the product meets the functional requirements.
- The function of the mechanical separator is to form and maintain a physical barrier between the plasma and blood cells post-centrifugation of the blood specimen (Figure 9-2). This barrier prevents the red blood cells from contaminating the analytes in the plasma from the products of cell lysis. The mechanical separator's density is less than that of blood cells but greater than plasma and remains positioned between the two layers.

Figure 9-1 Vacutainer® Barricor™ Plasma Blood Collection Tube

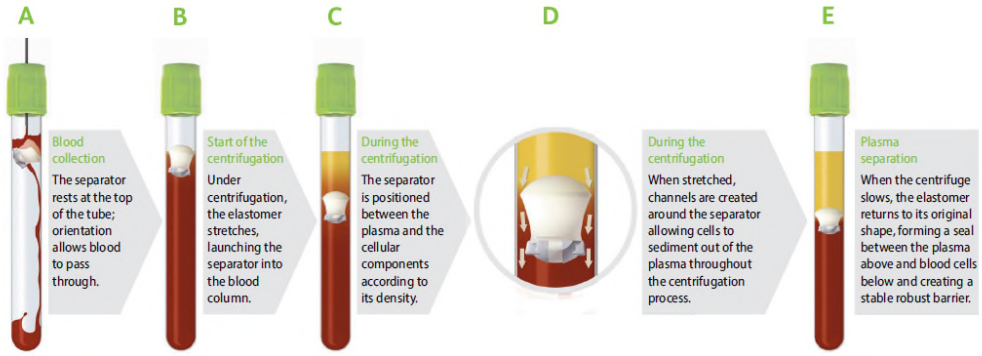

Figure 9-2 Blood collection and plasma separation with Vacutainer® Barricor™ Plasma Blood Collection Tube

9.1.3 Broad information on use applied for (use descriptor system)

Life cycle stage (LCS)	Use at industrial site
Sector of Use (SU)	SU20 (Health services)
Product Category (PC)	PC0 (Other: Health care products)
Process Category (PROC)	PROC1 (Delivery and Storage of Thermoplastic Elastomer (TPE) resin) PROC8b (Transfer of Thermoplastic Elastomer (TPE) resin – Loading into Moulder Machine) PROC 14 (Operating Moulder Machine) PROC8b (Loading of Mechanical Separator in Assembling Machine of Blood Collection Tubes) PROC8b (Waste Treatment) PROC19 (Sampling) PROC10 (Cleaning and Maintenance of Moulder Machine)
Environmental Release Category (ERC):	ERC5 (Manufacturing Mechanical Separator for Blood Collection Tubes) ERC12c (Use of Mechanical Separator at Industrial Site)
Technical Function (TF):	UV stabiliser

9.1.4 Overview of uses and exposure scenarios

Tonnage information:

Assessed tonnage: [redacted] [100-200] kg of UV-328 per year contained in ([redacted][10,000-30,000] kg of TPE resin, with a [redacted] [<1] % of UV-328 on TPE resin w/w). CBI 1 & 2

These values reflect the maximum amount per year expected of use of UV-328 for the requested review period.

The content of UV-328 in the TPE resin ranges from [redacted] to [redacted] [<1] % (w/w). The tonnage has been calculated assuming a worst case scenario of [redacted] [<1] % of UV-328 on the TPE resin w/w. CBI 1

Considering the worst case scenario and the content of [redacted] [0.1-0.6] g of TPE per mechanical separator, it results [redacted] [0.0009-0.0054] g of UV-328 per separator: CBI 1

[redacted] [0.0009-0.0054] g UV-328/separator CBI 1

Table 9-1 gives an overview on the amount of used UV-328 for the years 2019 to 2021 and the estimated values for 2022 to 2027, including the TPE resin volume for manufacturing blood collection tubes on the applicant´s site in Plymouth for the global market.

Table 9-2 gives an overview on the estimated amount of used UV-328 for the years 2022 to 2027, including the TPE resin volume for blood collection tubes placed on the UK market.

Possible deviations between the amount of UV-328 that is purchased per year and the amount of UV-328 that is calculated from the amount of blood collection tubes produced per year can be explained considering that purchased TPE is not always completely consumed in one year. It is stored and used up the following year.

Table 9-1 Tonnage information – manufacturing blood collection tubes for the global market and corresponding amount of UV-328

Year	Purchased Volume of TPE (kg) containing UV-328	Corresponding Volume of UV-328 (kg) incorporated in TPE from [redacted] %	Corresponding Volume of UV-328 (kg) incorporated in TPE to [redacted] %	Unit of blood collection tubes produced for the global market
2019	[redacted]	[redacted]	[redacted]	[redacted]
2020	[redacted]	[redacted]	[redacted]	[redacted]
2021	[redacted]	[redacted]	[redacted]	[redacted]
2022	[redacted]	[redacted]	[redacted]	[redacted]
2023	[redacted]	[redacted]	[redacted]	[redacted]
2024	[redacted]	[redacted]	[redacted]	[redacted]
2025	[redacted]	[redacted]	[redacted]	[redacted]
2026	[redacted]	[redacted]	[redacted]	[redacted]

CBI 1

Year	Purchased Volume of TPE (kg) containing UV-328	Corresponding Volume of UV-328 (kg) incorporated in TPE from [redacted] % to [redacted] %	Unit of blood collection tubes produced for the global market
2027	[redacted]	[redacted]	[redacted]

CBI 1

Table 9-2 Tonnage information – blood collection tubes placed on the UK market and corresponding amount of UV-328

Year	Unit of blood collection tubes placed on the UK market	Corresponding Volume of UV-328 (kg) ([redacted] [0.0009-0.0054] g UV-328/separator)
2022	[redacted]	[redacted]
2023	[redacted]	[redacted]
2024	[redacted]	[redacted]
2025	[redacted]	[redacted]
2026	[redacted]	[redacted]
2027	[redacted]	[redacted]

CBI 1

9.1.5 Process Description

The manufacturing process in place at Plymouth site is described as:

- Plymouth plant operates 24/7; 336 days per year. The site receives UV-328 as a component of a TPE resin in shipping containers (octabins), each octabin contains 290 kg of TPE resin.
- By following Good Receipt SOP in place at the site, the incoming raw material (TPE resin) arrives at the loading bay, then is unloaded by fork lift truck into the receiving area (5 to 20 meters away from the loading bay) by trained employees.
- The octabins containing the TPE resin is then moved to storage racking (20 to 80 meters away from the receiving area). The warehouse is secured from public access but open to trained site staff access.
- When TPE resin is ordered by production, then the octabin is brought to the moulding delivery airlock by fork lift (20 to 80 meters away from storage racking) and placed next to the moulding injection machine. Figure 9-3 below describes the moulding process.

CBI 1

Figure 9-3 Overview of moulding process involving the use of TPE resin as raw material

- Sealed plastic bags containing TPE resin are stored inside the octabin. One site operator cuts the bags containing the TPE resin at the top and pour the TPE resin content into the material infeed bin, which is then closed. This task is performed by trained employees without formation of dust and without dermal contact with TPE resin. Octabins and plastic bags are then properly managed as waste intended for incineration.

- The TPE resin is automatically loaded from the material infeed bin and delivered in the moulding injection machine (a vacuum wand is inserted and lifts the resin and deposits it directly to a hopper to feed the screw press). During the moulding process, the TPE resin is heated to [redacted] [200-240] ºC and moulded to obtain the proper shape and thickness.

  CBI 1

  The machine works under rigorously controlled conditions, being a closed system. Trained operators carry out sampling for quality control purposes, together with cleaning operations, by following specific SOPs.

- The moulding process ends with the production of the mechanical separator consisting of TPE (Figure 9-1). Mechanical separators are automatically collected and then stored in plastic bags in stacking crates prior to the next assembly stage.

- Plastic bags with mechanical separators are handled toward a lubricant drum and then poured in the assembling machine. They are then oriented correctly by vibration and mechanically inserted in the blood collection tubes by a pick and place head from a hopper.

9.1.6 Introduction to the assessment

The current CSR and the associated exposure scenarios support the application for authorisation of UV-328 as UV-stabiliser incorporated in thermoplastic

elastomer (TPE) resin for its industrial use to manufacture mechanical separators which are then inserted in blood collection tubes.

UV-328 has been included into Annex XIV of the REACH Regulation (list of substances subject to Authorisation) due to its intrinsic properties (PBT, vP and vB). According to Regulation (EC) No 1907/2006, Article 62(4)(d), the CSR supporting an application for Authorisation needs to cover only those risks arising from the intrinsic properties specified in Annex XIV. Therefore, only risks related to the classification of UV-328 as PBT and vPvB are addressed in this CSR.

9.1.6.1 Environment

Scope and type of assessment

Since UV-328 is classified for PBT and vPvB, reliable prediction of long-term exposure is not possible and an emission characterisation and risk characterisation has to be conducted. The outcome is the identification and implementation of risk management measures (RMM) which minimise the emission to the environment [8]. The present risk assessment does not include any calculation of risk characterisation based on a PNEC value. The objective of the present document is to show that emissions to the environment have been minimised using all technically feasible measures. The focus of this CSR is on the qualitative assessment of the required minimisation of the release of UV-328 into the environment. Data demonstrate that environmental releases of UV-328 are well controlled and no releases to the environment occur during the whole process. These data are reported in the environmental exposure scenario ES-EC1 in chapter 9.2.1 and 9.2.2.

9.1.6.2 Humans via environment

Scope and type of assessment

Quantitative risk assessment methodologies generally cannot be used for estimating the risk from a PBT /vPvB substance of indirect exposure of humans via the environment [9].

The present risk assessment does not include any calculation of risk characterisation for humans via environment. The objective of the present document is to show that emissions to the environment have been minimised using all technically feasible measures. The focus of this CSR is on the qualitative assessment of minimising the release of UV-328 into the environment and consequently also on minimising indirect exposure of humans via the environment. As described in chapter 9.1.5, releases of UV-328 to the environment are well controlled and data demonstrate that no releases to the environment occur during the whole process and therefore humans via the environment is not further assessed in this document.

The plasma blood collection tube, incorporating the mechanical separator, has no commercial applications for the general public, as these tubes are only delivered

to hospitals and medical professionals. At the end of life, the blood collection tube is disposed of as per the UK waste legislation as biohazardous waste via incineration

9.1.6.3 Workers

Scope and type of assessment

Although quantitative risk assessment methodologies generally cannot be used for estimating the risk of PBT /vPvB substance in the environment or to humans via the environment, they can be used for assessing the risk for workers.

For the purpose of this AfA, the assessment for workers relates to repeated dose toxicity. UV-328 meets the criteria for specific target organ toxicity – repeated exposure in sub-category 2 (STOT RE 2).

To demonstrate that workplace exposure does not result in a health risk, DNEL values derived from data obtained from repeated dose toxicity studies [2] are used for safety assessment. Where exposure to workers cannot be excluded, the risk is calculated with CHESAR Tool (version 3.7.1). If exposure can be excluded a qualitative assessment is conducted.

The scope of the exposure assessment and type of risk characterisation required for workers are described in Table 9-3.

Table 9-3 Type of risk characterisation required for workers (USE 1)

Route of exposure	Type of effect	Type of risk characterisation	Hazard conclusion
Inhalation	Systemic, long-term	Quantitative	DNEL 0.7 mg/m^3
Dermal	Systemic, long-term	Quantitative	DNEL 0.3 mg/kg bw/day

9.1.7 General information on risk management related to toxicological/ecotoxicological hazards

Operational conditions and risk management measures are provided in each of the contributing scenarios in chapter 9.2 below. The following risk management measures are implemented at the applicants' site:

a) No liquid waste containing UV-328 occurs during the process. Solid waste containing UV-328 is collected and incinerated.

b) Access to warehouse, laboratory and manufacturing areas is strictly controlled to prevent unauthorised access.

c) For all activities, Standard Operation Procedures (SOPs) are available according to GMP. All activities are tracked in a computer system and/or paper based documentation.

d) For all activities a good standard of occupational hygiene is implemented. Employees are trained and instructed, aware of the hazards and supervised to avoid any direct contact with UV-328 and to ensure that any UV-328-contaminated waste is collected for incineration.

e) Becton Dickinson has an integrated EHS management system in place which covers:

- Conformity with ISO 14001. The site was most recently re-certified in February 2019.
- Legal compliance assurance with support of a safety professional and a safety committee, which meets regularly.
- Workplace risk assessment for all tasks around the operations involving UV-328.
- Specific hazardous substances exposure and risk assessments for each task.
- Operational controls according to Becton Dickinson's corporate and internal requirements and standards.
- Job descriptions and a skills matrix, which ensures that for each task, workers have the required skill level, including verification of competencies.
- A training plan for technical workers to become familiar with the equipment.
- An incident investigation program.
- A requirement for regular inspections by the safety representatives, corporate safety audits and visits by the occupational physician.
- Annual training requirements, covering, in particular, chemical hazards, hygiene practices to prevent and minimise exposures and how to report any problems that may arise, is provided to all involved operators.

f) The following minimum standards for PPE (personal protective equipment) is used by employees at the Becton Dickinson site:

- Professional work clothing (trousers, jacket or overalls) which are removed after work and which are regularly cleaned.
- Safety shoes with acid resistant soles (EN ISO20345).
- A skin protection program (soap, protection ointment) is provided at all washing places and sinks.

- Gloves as per the internal program plan, for those operations with potential dermal contact with TPE resin, tested to Nitrile Disposable Gloves – EN 374-1:2016/Type B JKL, EN 374-5:2016 Virus, EN 388:2016 2.0.0.0.X, EN 455:2000 1.2.3.4.

- Chemical goggles, tested to EN ISO20345

g) The site has an established Emergency Response Program, which is regularly practiced. Drills are performed every two years, also including response to chemical accidents.

Detailed Description on waste incineration

Solid waste results from empty octabins, unusable batches, moulding and production waste (including defective products) and from cleaning and maintenance operations.

As described in this chapter, no liquid waste containing UV-328 occurs during the process, while solid waste containing or contaminated with UV-328 is incinerated.

- TPE resin containing UV-328 is stored in closed octabins from delivery until its use in moulding process. A spill procedures preventing escape to the local environment is in place at the shop floor and warehouse environment and neither emissions nor spillages have been recorded.

- Octabins are repurposed for waste storage after use and then incinerated with any waste content.

- TPE resin is used in a closed system from vacuum delivery to moulding machine. Solid waste material is mostly generated by the machine moulding process. Unusable mould waste is not treated on site. It is collected by a licensed vendor as a separate waste stream.

- Processing machines are regularly sanitised by using Isopropyl Alcohol (IPA) wipes, as a result no waste process water release can occur during the entire process.

- All measures have been implemented according to Best Practice. All efforts have been undertaken to ensure that UV-328 is not released in any amount into the environment.

For further information refer to chapters 9.2.1 and 9.2.2.

9.2 Exposure scenario ES1: Manufacturing Mechanical Separator for Blood Collection Tubes

Market sector / Product Category: PC0 (Other: Health Care Products)

Sector of use: SU20 (Health services)

Environment contributing scenario(s):

ECS1: ERC5 (Manufacturing Mechanical Separator for Blood Collection Tubes)

ECS2: ERC12c (Use of Mechanical Separator at Industrial Site)

Worker contributing scenario(s):

WCS1: PROC1 (Delivery and Storage of Thermoplastic Elastomer (TPE) Resin)

WCS2: PROC8b (Transfer of Thermoplastic (TPE) Resin – Loading into Moulder Machine)

WCS3: PROC14 (Operating Moulder Machine)

WCS4: PROC8b (Loading of Mechanical Separator in Assembling Machine of Blood Collection Tubes)

WCS5: PROC8b (Waste Treatment)

WCS6: PROC19 (Sampling)

WCS7: PROC10 (Cleaning and Maintenance of Moulder Machine)

Technical function(s): UV stabiliser

Article Category: AC13g (Other plastic article)

Consumer contributing scenario(s): not applicable

Subsequent service life exposure scenario(s): Yes

Description of the activities and technical processes covered in the exposure scenario:

A general description of the activities and technical processes is given in chapter 9.1.4. Further details on activities and processes in the respective contributing scenarios are provided in chapter 9.2.

9.2.1 ES1 – ECS1: Manufacturing Mechanical Separator for Blood Collection Tubes

9.2.1.1 Conditions of use

Product (article) characteristics
• Thermoplastic elastomer (TPE) resin containing UV-328
Amount used, frequency and duration of use
• Annual use at site: [redacted] [10,000-30,000] kg of TPE resin with concentration of [redacted] [<1]%wt UV-328 ([redacted] [10-200] kg UV-328) Detailed tonnage data are presented in Table 9-1 and Table 9-2. • Daily use at site (UV-328): [redacted] [0.1-0.5] g UV-328 / day (worst case value based on [redacted] [<1] %wt) Operation days: 336 days/year
Technical and organisational conditions and measures
• General organisational conditions are described in chapter 9.1.7 • An overview of the production process at the applicant´s site is given in Figure 9-3. All production processes involving the use of TPE resin are conducted in closed systems.
Conditions and measures related to sewage treatment plant
• Not applicable as no waste water is generated during the entire process.
Conditions and measures related to treatment of waste
• Solid material containing UV-328 is classified and treated as hazardous waste according to UK regulations. • Any solid waste resulting from on-site waste treatment is sent to an external waste management company (licensed contractor) for disposal via incineration as hazardous waste. Therefore no emissions arise from the waste path. • Solid waste generates from: o Unused TPE batches o Contaminated octabins o TPE waste from the moulding process (including defective products) o Cleaning activities
Other conditions affecting environmental exposure.
• None
Conditions and measures related to treatment of exhaust air
• For general ventilation of the operating area, fresh air is supplied with a total throughput of 28,926 m3/h (8.035 m3/s) via the central air conditioning system.

CBI 1 & 2

Explanation of the approach taken for the exposure scenario:

TPE resin containing UV-328 is used under rigorously controlled conditions throughout the entire manufacturing process of the mechanical separator, starting with the delivery, storage, during transfer to the moulding machine (that is located in air locked room (Figure 9-4) and that is encapsulated (Figure 9-5)), up to the automatic collection of mechanical separates in plastic bags and their storage for future assembling.

Solid waste containing UV-328 is collected and sent to an external waste management company (licenced contractor) for disposal as hazardous waste. There is no liquid waste or wastewater containing UV-328.

During the manufacturing process there is no release of UV-328 into the environment.

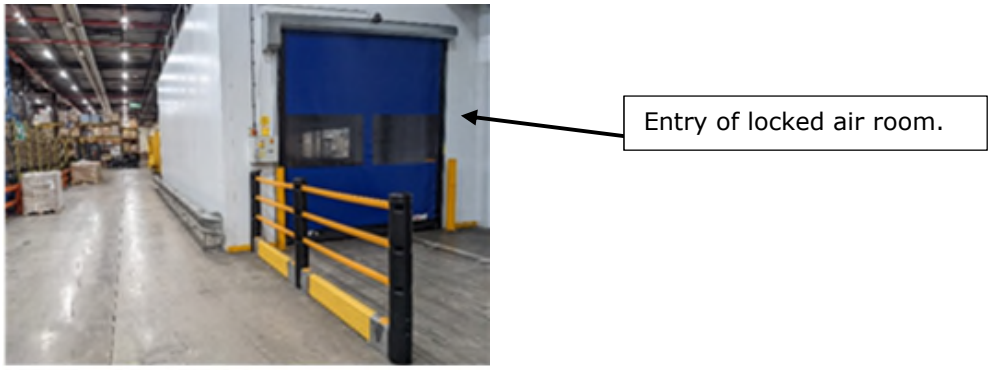

Figure 9-4 Air locked room, location of moulding machine

Figure 9-5 Moulding machine encapsulated with local exhaust

9.2.1.2 Releases

Table 9-4 Operational conditions affecting local releases to the environment

Operational conditions	
Annual site tonnage	[redacted] [100-200] kg UV-328
Daily amount used at site	[redacted] [0.1-0.5] g UV-328
Releases times per year	0
Release fraction to air from process	0 (justification: Emission to air are negligible because of the low vapour pressure of the substance 0.000005 Pa at 20°C (ECHA, 2022)
Release fraction to wastewater from process	0 (justification: No emission from wastewater is expected, because no waste water occurs during the entire process including during cleaning)
Release fraction to soil from process	0 (justification: No emission to soil is expected, because no waste water occurs during the entire process and waste is incinerated)

CBI 2

Releases to Waste

Release factor of waste from the process: 0 %

The following waste is generated at the applicant`s site related to UV-328:

- Used octabins
- TPE waste from the moulding process (including rejected products)
- Unused batches
- IPA used for cleaning activities

Waste occurring from the moulding machine is approximately 8% of the total amount of waste generated at site. As described in chapter 9.2.1, this waste is collected and disposed as hazardous waste via incineration by an external waste management company (licensed contractor).

Table 9-5 quantifies the annual records of TPE waste produced during the moulding process for the years 2015 to 2021.

Table 9-5 Annual record of TPE waste from moulding machine - 8% of the total amount of waste generated at site

Year	Waste of TPE (kg) resulting from moulding process
2015	[redacted]
2016	[redacted]
2017	[redacted]
2018	[redacted]
2019	[redacted]
2020	[redacted]
2021	[redacted]

CBI 1

9.2.1.3 Exposure to the environment

As described in chapter 9.1 and 9.2, exposure to the environment is not expected.

9.2.2 ES1 – ECS2: Use Mechanical Separator at Industrial Site

The mechanical separator falls under the definition of an article according to UK REACH. The inclusion of the separator in the blood tube is not a use for AfA purposes. Discarded separators are disposed of as hazardous waste via incineration by a licensed contractor.

9.2.2.1 Exposure to the environment - end of life

At end of life, the final article (used blood tube) is disposed of as biohazardous waste via incineration. Exposure to the environment is not expected.

9.2.3 ES1 – WCS1: Delivery and Storage of Thermoplastic Elastomer (TPE) resin (PROC1)

At the applicant's site in Plymouth (UK), the TPE resin incorporating UV-328 is delivered once per month in octabins (Figure 9-6). The TPE resin is in sealed bags in the octabins. Octabins are unloaded and transferred into the warehouse (Figure 9-7) by a trained employee. They are kept in separate, lockable areas. There is no potential for exposure.

Figure 9-6 Octabin containing UV-328 incorporated in TPE

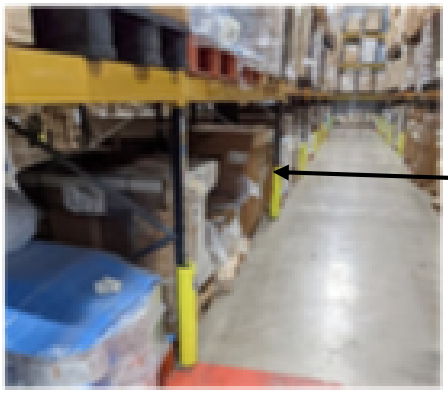

Figure 9-7 Octabin stored in warehouse

9.2.3.1 Conditions of Use

	Method
Product (Article) characteristics	
• Percentage (w/w) of substance in mixture/article: [redacted] [<1]%	Qualitative
• Physical form of the used product: Solid (material with no or very low dustiness)	Qualitative
Amount used (or contained in articles), frequency and duration of use/exposure	
• Duration of activity: <= 0.025 h/day *30 min/month*	Qualitative
Technical and organisational conditions and measures	
• Room ventilation: Enhanced (5 to 10 ACH) [Effectiveness Inhalation: 70%]	Qualitative
• Occupational Health and Safety Management System: Advanced	Qualitative
• Local exhaust ventilation: No [Effectiveness Inhalation: 0%, Dermal: 0%]	Qualitative
Conditions and measures related to personal protection, hygiene and health evaluation	
• Respiratory protection: No [Effectiveness Inhalation: 0%]	Qualitative

CBI 1

	Method
• Dermal protection: No [Effectiveness Dermal: 0%]	Qualitative
Other conditions affecting workers exposure	
• Place of use: Indoor (Room 100-1000 m3)	Qualitative
• Operating temperature: <= 40.0 °C	Qualitative

9.2.3.2 Exposure and Risks for Workers

The exposure concentrations and risk characterisation ratios (RCR) are presented in the following table.

Table 9-6 Exposure concentrations and risks for workers

Route of exposure and type of effects	Exposure concentration	Risk quantification
Inhalation, systemic, long term	0 (qualitative)	0 (qualitative)
Dermal, systemic, long term	0 (qualitative)	0 (qualitative)
Combined routes, systemic, long-term		0 (qualitative)

Remarks on exposure dataset obtained with ECETOC TRA

Risk is assessed qualitatively since no exposure.

Risk characterisation

No risk expected for workers related to this activity.

9.2.4 ES1 – WCS2: Transfer of Thermoplastic Elastomer (TPE) Resin – Loading into Moulder Machine (PROC8B)

An Octabin containing TPE is transferred from the warehouse to the moulder machine, located in an air locked room (Figure 9-4), and left next to the infeed bin (Figure 9-8). The Operator unseals the TPE bag and put it upended into the feeding bin, pulls the empty bag out and then closes the bin (Figure 9-9 and 9-8). A vacuum wand is inserted into the bin. Vacuum lifts the resin and deposits it directly onto a hopper to feed the screw press. During the task, no dust is generated as the granules is a soft, gel-like material.

The transfer of TPE resin to the feeding bin it is performed by one worker and takes around 20 minutes per week.

CBI 1

Figure 9-8 Octabin left next to the infeed bin

CBI 1

Figure 9-9 Transfer process of TPE from Octabin into the infeed bin

9.2.4.1 Conditions of Use

	Method
Product (Article) characteristics	
• Percentage (w/w) of substance in mixture/article: <= [redacted] [<1]%	TRA Workers 3.0
• Physical form of the used product: Solid (material with no or very low dustiness)	TRA Workers 3.0
Amount used (or contained in articles), frequency and duration of use/exposure	
• Duration of activity: 0.066 h/day *20 min/week*	TRA Workers 3.0
Technical and organisational conditions and measures	
• General ventilation: Enhanced (5 to 10 ACH) [Effectiveness Inhalation: 70%]	TRA Workers 3.0
• Occupational Health and Safety Management System: Advanced	TRA Workers 3.0
• Local exhaust ventilation: No [Effectiveness Inhalation: 0%, Dermal: 0%]	TRA Workers 3.0
Conditions and measures related to personal protection, hygiene and health evaluation	
• Respiratory protection: No [Effectiveness Inhalation: 0%]	TRA Workers 3.0
• Dermal protection: Chemical resistant dermal protection with specific employee training. (effectiveness = 95%) *Gloves (Nitrile Disposable Gloves – EN 374-1:2016/Type B JKL, EN 374-5:2016 Virus, EN 388:2016 2.0.0.0.X, EN 455:2000 1.2.3.4.)*	TRA Workers 3.0
Other conditions affecting workers exposure	
• Place of use: Indoor (Room 100-1000 m3)	TRA Workers 3.0
• Operating temperature: <= 40.0 °C	TRA Workers 3.0

CBI 1

9.2.4.2 Exposure and Risks for Workers

The exposure concentrations and risk characterisation ratios (RCRs) are reported in the following table.

Table 9-7 Exposure concentrations and risks for workers

Route of exposure and type of effects	Exposure concentration	Risk quantification
Inhalation, systemic, long term	3E-4 mg/m³ (TRA Workers)	RCR < 0.01
Dermal, systemic, long term	6.86E-3 mg/kg bw/day (TRA Workers)	RCR = 0.023

Route of exposure and type of effects	Exposure concentration	Risk quantification
Combined routes, systemic, long-term		RCR = 0.023

Remarks on exposure dataset obtained with ECETOC TRA

The vapour pressure at operating temperature (40°C) used for the calculation is 1.85E-5 Pa. Local exhaust ventilation effectiveness used by TRA: inhalation 0 %.

Risk characterisation

Risk related to this activity is controlled RCR <1.

9.2.5 ES1 – WCS3: Operating Moulder Machine (PROC14)

TPE resin is automatically directed toward the moulding machine (Figure 9-5).

The moulding process consists of two injection shots. The first injection shot consists of a PP (polypropylene) material injection while the second injection shot consists of a TPE resin injection. During the second shot the TPE resin is heated and shaped into a mechanical separator. The moulding process ends with the production of the mechanical separator consisting of TPE. Mechanical separators are articles. These articles are automatically collected in the collecting bins and then stored in plastic bags in stacking crates prior to their assembly into the blood collection tubes (Figure 9-1).

The entire moulding process is carried out in a fully enclosed moulding machine (Figure 9-6). There is no potential for worker exposure during the moulding process. The only possibility of exposure is when the encapsulation of the moulding machine is opened and enclosed air can escape. Due to the low vapour pressure of the substance, exposure can be considered negligible. However as a worst case scenario, exposure and risk of the workers via inhalation is calculated. For the risk calculation, a maximum of 8 hours and a temperature of <= 80°C are used.

9.2.5.1 Conditions of Use

	Method
Product (Article) characteristics	
• Percentage (w/w) of substance in mixture/article: [redacted] [<1]%	Qualitative / TRA Workers 3.0
• Physical form of the used product: Solid (material with no or very low dustiness)	Qualitative / TRA Workers 3.0
Amount used (or contained in articles), frequency and duration of use/exposure	
• Duration of activity: <= 8 h/day	Qualitative / TRA Workers 3.0

CBI 1

	Method
Technical and organisational conditions and measures	
• General ventilation: Enhanced (5 to 10 ACH) [Effectiveness Inhalation: 70%]	Qualitative / TRA Workers 3.0
• Occupational Health and Safety Management System: Advanced	Qualitative / TRA Workers 3.0
• Local exhaust ventilation: No [Effectiveness Inhalation: 0%, Dermal: 0%]	Qualitative / TRA Workers 3.0
Conditions and measures related to personal protection, hygiene and health evaluation	
• Respiratory protection: No [Effectiveness Inhalation: 0%]	Qualitative / TRA Workers 3.0
• Dermal protection: No [Effectiveness Dermal: 0%]	Qualitative / TRA Workers 3.0
Other conditions affecting workers exposure	
• Place of use: Indoor (Room 100-1000 m3)	Qualitative / TRA Workers 3.0
• Operating temperature: [redacted] [200-240] °C (process temperature); <=80°C (maximum temperature opening the encapsulation)	Qualitative / TRA Workers 3.0

CBI 1

9.2.5.2 Exposure and Risks for Workers

The exposure concentrations and risk characterisation ratios (RCRs) related to this activity are presented in the following table.

Table 9-8 **Exposure concentrations and risks for workers**

Route of exposure and type of effects	Exposure concentration	Risk quantification
Inhalation, systemic, long term	3E-3 mg/m³ (TRA Workers)	RCR < 0.01
Dermal, systemic, long term	0 (qualitative)	0 (qualitative)
Combined routes, systemic, long-term		RCR < 0.01

Remarks on exposure dataset obtained with ECETOC TRA

The vapour pressure at operating temperature (80°C) used for the calculation is 1E4 Pa.

Local exhaust ventilation effectiveness used by TRA: inhalation 0 %.

Risk characterisation

Risk related to this activity is controlled RCR <1.

9.2.6 ES1 – WCS4: Loading of Mechanical Separators in Assembling Machine of Blood Collection Tubes (PROC8b)

The mechanical separator is the core of the Vacutainer® Barricor™ Plasma Blood Collection Tubes (Figure 9-1).

The mechanical separator is defined as an article according to UK REACH and the use of an article which contains Annex XIV substance is not subject to the authorisation requirement. However, for the sake of completeness a use description is provided in this chapter.

Without direct contact with the operators, plastic bags with mechanical separators are handled into a lubricant drum and then poured in the assembling machine (Figure 9-10). The mechanical separators are automatically added to a supply hopper (Figure 9-11) and delivered to a pick and place head in correct orientation via vibratory shuts (Figure 9-12).

The pick and place head places the separators in carriages which deliver the separators to the insertion head. Separators are collapsed, inserted into the head to the correct depth and oriented to the correct operating position (Figure 9-13).

The process ends with the production of Vacutainer® Barricor™ Plasma Blood Collection Tubes.

There is no direct interaction with the separators during this activity, with the exception of clearing jams in the production line during which gloves are used.

CBI 1

Figure 9-10 Drum for lubrication of mechanical separator

CBI 1

Figure 9-11 Loading of mechanical separators in the assembling machine

CBI 1

Figure 9-12 Vibratory shuts for the correct orientation of mechanical separators

CBI 1

Figure 9-13 Insertion process of the mechanical separator

9.2.6.1 Conditions of Use

	Method
Product (Article) characteristics	
• Percentage (w/w) of substance in mixture/article: [redacted] [<1]%	not applicable
• Physical form of the used product: Solid (article)	not applicable
Amount used (or contained in articles), frequency and duration of use/exposure	
• Duration of activity: <= 2 h/day	not applicable
Technical and organisational conditions and measures	
• General ventilation: Enhanced (5 to 10 ACH) [Effectiveness Inhalation: 70%]	not applicable
• Occupational Health and Safety Management System: Advanced	not applicable
• Local exhaust ventilation: No [Effectiveness Inhalation: 0%, Dermal: 0%]	not applicable
Conditions and measures related to personal protection, hygiene and health evaluation	
• Respiratory protection: No [Effectiveness Inhalation: 0%]	not applicable
• Dermal protection: No [Effectiveness Dermal: 0%]	not applicable
Other conditions affecting workers exposure	
• Place of use: Indoor (Room 100-1000 m3)	not applicable
• Operating temperature: <= 40.0 °C	not applicable

CBI 1

9.2.6.2 Exposure and Risks for Workers

Exposure and risk assessment of using the separator is not required within the framework of this authorisation application. However, as described above, there is no exposure to the substance, thus any risk related to this activity is controlled.

9.2.7 ES1 – WCS5: Waste treatment (PROC8b)

Solid waste, containing UV-328 as a component of TPE, is mainly generated during the injection moulding process which takes place at the shop floor. Solid waste can also be generated during sampling and cleaning activities and in case of spillages (which have never been recorded). A spill procedure preventing escape to the local environment is in place at the shop floor and warehouse environment.

Waste is collected in closed octabins (reusing of the shipping octabins), which are sent to the waste skip immediately once filled and disposed of via a licensed waste management company, as described in chapter 9.1 and 9.2. Waste is entirely managed under ISO14001.

No liquid waste occurs during the entire manufacturing process.

Under the worst case scenario, up to six workers are involved in this activity. 1 hour per week is estimated for the activity related to handling waste containing UV-328.

9.2.7.1 Condition of Use

	Method
Product (Article) characteristics	
• Percentage (w/w) of substance in mixture/article: [redacted] [<1]%	TRA Workers 3.0
• Physical form of the used product: Solid (material with no or very low dustiness)	TRA Workers 3.0
Amount used (or contained in articles), frequency and duration of use/exposure	
• Duration of activity: <= 0.2 h/day *1 hour/week*	TRA Workers 3.0
Technical and organisational conditions and measures	
• General ventilation: Enhanced (5 to 10 ACH) [Effectiveness Inhalation: 70%]	TRA Workers 3.0
• Occupational Health and Safety Management System: Advanced	TRA Workers 3.0
• Local exhaust ventilation: No [Effectiveness Inhalation: 0%, Dermal: 0%]	TRA Workers 3.0
Conditions and measures related to personal protection, hygiene and health evaluation	
• Respiratory protection: No [Effectiveness Inhalation: 0%]	TRA Workers 3.0
• Dermal protection: Chemical resistant dermal protection with specific employee training. (effectiveness = 95%) *Gloves (Nitrile Disposable Gloves – EN 374-1:2016/Type B JKL, EN 374-5:2016 Virus, EN 388:2016 2.0.0.0.X, EN 455:2000 1.2.3.4.)*	TRA Workers 3.0

CBI 1

	Method
Other conditions affecting workers exposure	
• Place of use: Indoor (Room 100-1000 m3)	TRA Workers 3.0
• Operating temperature: <= 40.0 °C	TRA Workers 3.0

9.2.7.2 Exposure and Risks for Workers

The exposure concentrations and risk characterisation ratios (RCRs) are reported in the following table.

Table 9-9 Exposure concentrations and risks for workers

Route of exposure and type of effects	Exposure concentration	Risk quantification
Inhalation, systemic, long term	3E-4 mg/m³ (TRA Workers)	RCR < 0.01
Dermal, systemic, long term	6.86E-3 mg/kg bw/day (TRA Workers)	RCR = 0.023
Combined routes, systemic, long-term		RCR = 0.023

Remarks on exposure dataset obtained with ECETOC TRA

The vapour pressure at operating temperature (40°C) used for the calculation is 1.85E-5 Pa.

Local exhaust ventilation effectiveness used by TRA: inhalation 0 %

Risk characterisation

The risk related to this activity is controlled; RCR <1.

9.2.8 ES1 – WCS6: Sampling (PROC19)

Quality assurance and quality control operations are required in different parts of the manufacturing process, as prescried by GMP and described in specific SOPs.

Raw material: On receipt of the TPE resin raw material (once a month), the Software Quality Assurance (SQA) technician and chemistry technician are responsible for qualtiy control.

Production of the mechanical separator: During the moulding process, the moulding operator regularly checks the pruduction of mechanical separators both vissually and though manual sampling.

The entire activity involves up to ten workers, 2 hours per week per worker. These values also includes the quality control of the mechanical separator, defined as article according to UK REACH.

9.2.8.1 Condition of Use

	Method
Product (Article) characteristics	
• Percentage (w/w) of substance in mixture/article: [redacted] [<1]%	TRA Workers 3.0
• Physical form of the used product: Solid	TRA Workers 3.0
Amount used (or contained in articles), frequency and duration of use/exposure	
• Duration of activity: <= 0.4 h/day *2 hours/week*	TRA Workers 3.0
Technical and organisational conditions and measures	
• General ventilation: Enhanced (5 to 10 ACH) [Effectiveness Inhalation: 70%]	TRA Workers 3.0
• Occupational Health and Safety Management System: Advanced	TRA Workers 3.0
• Local exhaust ventilation: No [Effectiveness Inhalation: 0%, Dermal: 0%]	TRA Workers 3.0
Conditions and measures related to personal protection, hygiene and health evaluation	
• Respiratory protection: No [Effectiveness Inhalation: 0%]	TRA Workers 3.0
• Dermal protection: Chemical resistant dermal protection with specific employee training. (effectiveness = 95%) *Gloves (Nitrile Disposable Gloves – EN 374-1:2016/Type B JKL, EN 374-5:2016 Virus, EN 388:2016 2.0.0.0.X, EN 455:2000 1.2.3.4.)*	TRA Workers 3.0
Other conditions affecting workers exposure	
• Place of use: Indoor (Room 100-1000 m3)	TRA Workers 3.0
• Operating temperature: <= 40.0 °C	TRA Workers 3.0

CBI 1

9.2.8.2 Exposure and Risks for Workers

The exposure concentrations and risk characterisation ratios (RCR) are reported in the following table.

Table 9-10 **Exposure concentrations and risks for workers**

Route of exposure and type of effects	Exposure concentration	Risk quantification
Inhalation, systemic, long term	3E-3 mg/m³ (TRA Workers)	RCR < 0.01
Dermal, systemic, long term	0.141 mg/kg bw/day (TRA Workers)	RCR = 0.471

Route of exposure and type of effects	Exposure concentration	Risk quantification
Combined routes, systemic, long-term		RCR = 0.476

Remarks on exposure dataset obtained with ECETOC TRA

The vapour pressure at operating temperature (40°C) used for the calculation is 1.85E-5 Pa.

Local exhaust ventilation effectiveness used by TRA: inhalation 0 %

Risk characterisation

Risk related to this activity is controlled RCR <1.

9.2.9 ES1 – WCS7: Cleaning and Maintenance of Moulder Machine (PROC10)

Cleaning and maintenance operations are regularly carried out on site. Evidence of completion of cleaning is stored in the device history records.

The production line is cleaned with liquid IMS from a spray bottle used with lint free cloths at every line clearance and during routine preventive maintenance. IPA wipes are used for cleaning operations. The line is also treated with paired biocides every 3 weeks with HCL acid and 1 week Spor-Klenz®.

Up to four trained workers are appointed for cleaning and maintenance operation, 1 hour per day per worker.

9.2.9.1 Condition of Use

	Method
Product (Article) characteristics	
• Percentage (w/w) of substance in mixture/article: [redacted] [<1]%	TRA Workers 3.0
• Physical form of the used product: Solid (material with no or very low dustiness)	TRA Workers 3.0
Amount used (or contained in articles), frequency and duration of use/exposure	
• Duration of activity: <= 1 h/day	TRA Workers 3.0
Technical and organisational conditions and measures	
• General ventilation: Enhanced (5 to 10 ACH) [Effectiveness Inhalation: 70%]	TRA Workers 3.0
• Occupational Health and Safety Management System: Advanced	TRA Workers 3.0
• Local exhaust ventilation: No [Effectiveness Inhalation: 0%, Dermal: 0%]	TRA Workers 3.0

CBI 1

	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
• Respiratory protection: No [Effectiveness Inhalation: 0%]	TRA Workers 3.0
• Dermal protection: Chemical resistant dermal protection with specific employee training. (effectiveness = 95%) *Gloves (Nitrile Disposable Gloves – EN 374-1:2016/Type B JKL, EN 374-5:2016 Virus, EN 388:2016 2.0.0.0.X, EN 455:2000 1.2.3.4.)*	TRA Workers 3.0
Other conditions affecting workers exposure	
• Place of use: Indoor (Room 100-1000 m3)	TRA Workers 3.0
• Operating temperature: <= 40.0 °C	TRA Workers 3.0

9.2.9.2 Exposure and Risks for Workers

The exposure concentrations and risk characterisation ratios (RCRs) are reported in the following table.

Table 9-11 **Exposure concentrations and risks for workers**

Route of exposure and type of effects	Exposure concentration	Risk quantification
Inhalation, systemic, long term	3E-3 mg/m³ (TRA Workers)	RCR < 0.01
Dermal, systemic, long term	0.027 mg/kg bw/day (TRA Workers)	RCR = 0.091
Combined routes, systemic, long-term		RCR = 0.096

Remarks on exposure dataset obtained with ECETOC TRA

The vapour pressure at operating temperature (40°C) used for the calculation is 1.85E-5 Pa.

Local exhaust ventilation effectiveness used by TRA: inhalation 0 %

Risk characterisation

Risk related to this activity is controlled RCR <1.

10 RISK CHARACTERISATION RELATED TO COMBINED EXPOSURE

10.1 Environment

No release of UV-328 into the environment is expected from the exposure scenario covered by this application for authorisation.

10.2 Human health

10.2.1 Workers

The use of TPE resin in the production of Vacutainer® Barricor™ Plasma Blood Collection Tubes, has been divided into 7 WCS (Table 10-1 and 10-2). As worst case scenario for risk characterisation combine exposure of activities is calculated. (Table 10-3).

Table 10-1 **Overview of worker inhalation exposure to UV-328**

Scenario	PROC	Method	Duration of activity (h/day)	Exposure estimate – Inhalation, systemic, long term (mg/m3)	Risk characterisation (RCR)
WCS1: Delivery and Storage of Thermoplastic Elastomer (TPE) Resin	1	Qualitative	0.025	0	0
WCS2: Transfer of Thermoplastic Elastomer (TPE) Resin - Loading into Moulder Machine	8b	TRA Workers	0.066	0.0003	<0.01
WCS3: Operating Moulder Machine Separator	14	TRA Workers	8	0.003	<0.01

Scenario	PROC	Method	Duration of activity (h/day)	Exposure estimate – Inhalation, systemic, long term (mg/m3)	Risk characterisation (RCR)
WCS4: Loading of Mechanical Separator in Assembling Machine of Blood Collection Tubes	8b	The mechanical separator is defined as an article according to UK REACH and the use of an article which contains Annex XIV substance is not subject to the authorisation requirement			
WCS5: Waste treatment	8b	TRA Workers	0.2	0.0003	<0.01
WCS6: Sampling	19	TRA Workers	0.4	0.003	<0.01
WCS7: Cleaning and Maintenance of Moulder Machine	10	TRA Workers	1	0.003	<0.01

Table 10-2 **Overview of worker dermal exposure to UV-328**

Scenario	PROC	Method		Exposure estimate – dermal, systemic, long term (mg/kg bw/day)	Risk characterisation (dermal)
WCS1: Delivery and Storage of Thermoplastic Elastomer (TPE) Resin	1	Qualitative	0.025	0	0

Scenario	PROC	Method		Exposure estimate – dermal, systemic, long term (mg/kg bw/day)	Risk characterisation (dermal)
WCS2: Transfer of Thermoplastic Elastomer (TPE) Resin - Loading into Moulder Machine	8b	TRA Worker	0.066	0.00686	0.023
WCS3: Operating Moulder Machine Separator	14	Qualitative	8	0	0
WCS4: Loading of Mechanical Separator in Assembling Machine of Blood Collection Tubes	8b	The mechanical separator is defined as an article according to UK REACH and the use of an article which contains Annex XIV substance is not subject to the authorisation requirement			
WCS5: Waste treatment	8b	TRA Worker	0.2	0.00686	0.023
WCS6: Sampling	19	TRA Worker	0.4	0.141	0.471
WCS7: Cleaning and Maintenance of Moulder Machine	10	TRA Worker	1	0.027	0.091

Table 10-3 **Overview of combined worker inhalation and dermal exposure to UV-328**

Scenario	Route of exposure	Exposure estimate (mg/kg bw/day)	Risk characterisation (RCR)
WCS1 + WCS2 + WCS3 + WCS5 + WCS 6 + WCS7	inhalation	0.0096 mg/m³	0.014
WCS1 + WCS2 + WCS3 + WCS5 + WCS6 + WCS7	dermal	0.182 mg/kg bw/day	0.606

Risk related to each activity is controlled as it can be demonstrated that all RCR values are below 1.

Risk related to combined activity is controlled as it can be demonstrated that the RCR value for dermal and inhalation are both below 1.

A refinement of the assessment from a qualitative perspective, supports the absence of risk for worker for the following reasons:

Both the UV-328 dermal and inhalation exposure can be considered unlikely because of:

1) the chemical-physical properties of the substance and the TPE resin and
2) the conditions of use of TPE resins, with specific regards to the temperature of use.

REFERENCES

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[9] Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.11: PBT/vPvB assessment; Version 3.0; EHCA; 2017

[10] Describing uses of additives in plastic material for articles and estimating related exposure Practical Guide for Industry; ECHA, March 2020

ANNEX I – JUSTIFICATIONS FOR CONFIDENTIALITY CLAIMS

Blanked out item reference	Justification for confidentiality
CBI 1	**Demonstration of Commercial Interest:** Proprietary manufacturing and specification information are closely held to prevent competitors from replicating procedures and procedures conditions. These details are only shared under strong non-disclosure agreements and are not made publicly available. **Demonstration of Potential Harm:** If process information were to be revealed, competitors could try to copy the design and process, leading to loss of knowhow and market position. Even a portion of the full process information or the applicant's specifications could be used to "reverse engineer" the process. **Limitation to Validity of Confidentiality:** This claim is valid indefinitely
CBI 2	**Demonstration of Commercial Interest:** Volumes of UV-328 imported and used are confidential information that are only to be used for the applicant's planning and operations. Sharing them publicly may also breach anti-trust and competition laws in the UK. **Demonstration of Potential Harm:** If competitors got hold of this information, they could use it to determine the applicant's output and market share or the weight of the particular products on their overall business. Competitors could use such sensitive information to gain a competitive advantage over the applicant. Some of the redacted information could also be used to back-calculate sensitive information. **Limitation to Validity of Confidentiality:** This claim is valid indefinitely