CHEMICAL SAFETY REPORT

PUBLIC

Legal name of applicant:	Becton, Dickinson U.K. Limited
Submitted by:	Becton, Dickinson U.K. Limited
Substance:	4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-OPnEO); Generic class: no EC or CAS number allocated
Use title:	Use of 4-(1,1,3,3 tetramethylbutyl)phenol, ethoxylated (4-tert-OPnEO)) for the lysis of different types of cells in order to release the cell contents for subsequence analysis in diagnostics
Use number:	1

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ABBREVIATIONS

Abbreviation	Definition
AfA	Application for Authorisation
AoA	Analysis of Alternatives
BD	Becton, Dickinson U.K. Limited
CBI	Confidential Business Information
CRO	Contract Research Organisations
CSR	Chemical Safety Report
DNEL	Derived No Effect Level
DU	Downstream user
ECS	Environmental Contributing Scenario
EEA	European Economic Area
EU	European Union
ERC	Environmental Release Category
EWC	European Waste Catalogue
FDA	Food and Drug Administration
HPV	Human Papilloma Virus
HSE	Health and Safety Executive
IFU	Instructions for Use
IVD	In vitro diagnostic medical device
LADs	Latest application dates
LCS	Life Cycle Stage
LUO	Laboratory Use Only
MDR	Medical Devices Regulation
MHRA	Medicines and Healthcare products Regulatory Agency
NP	Nonylphenol
NPnEO	Nonylphenol Ethoxylates
OC	Operational Conditions
OP	Octylphenol
OPnEO	Octylphenol Ethoxylates
PC	Product Category
PCR	Polymerase Chain Reaction
PNEC	Predicted No-Effect Concentration
PPE	Personal Protective Equipment
PROC	Process Category
REACH	Registration, Evaluation, Authorisation & Restriction of Chemicals
RCR	Risk Characterisation Ratio
RMM	Risk Management Measures
RSV	Respiratory Syncytial Virus
RUO	Research Use Only
SBT	Sample Buffer Tube
SD	Sunset date

Abbreviation	Definition
SU	Sector of Use
SEA	Socio-Economic Analysis
STI	Sexually Transmitted Infection
STP	Sewage Treatment Plant
SVHC	Substance of Very High Concern
UK	United Kingdom
UVCB	Unknown or Variable composition, Complex reaction products or Biological materials
WWTP	Wastewater Treatment Plant

DECLARATION

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

Also, we request that the information blanked out in the "public version" of the Chemical Safety Report (CSR) is not disclosed. We hereby declare that, to the best of our knowledge as of today (27 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 the third party whose commercial interests are at stake.

Daniel Hopkin

Director – Becton, Dickinson U.K. Limited

Winnersh, 27 June 2022

PART A

SUMMARY OF RISK MANAGEMENT MEASURES

The use of 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-OPnEO)) as a processing aid in imported diagnostics has been assessed in part B of this chemical safety report.

4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated covering well-defined substances and UVCB substances, polymers and homologues is classified as having endocrine disrupting properties (UK REACH, Article 57(f) - environment). As a non-threshold substance, this AfA has proceeded down the socio-economic route.

Becton, Dickinson U.K. Limited (hereafter referred to as 'Becton Dickinson' or ´BD´) imports diagnostics containing OPnEO and distributes to customers within the United Kingdom (UK). Risk Management Measures (RMM) have been communicated to customers via the technical data sheets and other product information.

Following UK REACH, Article 62(4)(d), the Chemical Safety Report (CSR) supporting an AfA needs to cover only those potential risks arising from the intrinsic properties specified in Annex XIV. Accordingly, only the potential impacts to the environment related to the emission of 4-tert-OPnEO, and its breakdown product 4-tert-Octyl Phenol (OP), are considered in the current CSR.

The use of 4-tert-OPnEO for the lysis of different types of cells in order to release the cell contents for subsequence analysis in diagnostics 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 exposure is provided below in the "Succinct Summary".

SUCCINCT SUMMARY OF REPRESENTATIVE RISK MANAGEMENT MEASURES (RMM) AND OPERATIONAL CONDITIONS (OC)

The use of 4-(1,1,3,3 tetramethylbutyl)phenol, ethoxylated ('OPnEO')) for the lysis of different types of cells in order to release the cell contents for subsequence analysis in diagnostics.

ECS and LCS	Task (ERC / PROC)	Annual amount of OPnEO placed on the UK market (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	Other conditions	Effectiveness of wastewater and waste air treatment (for ERC)	Release factors: water, air and soil (for ERC)	Detailed info. in CSR (section)	
ECS 1- Used as a processing aid in imported diagnostics	ERC 8a	[redacted][1E-02 – 10E-02]	• BD do not use diagnostics • Total volume of OPnEO imported into the UK spread across the DU present in the UK • OPnEO is contained within the diagnostic • Very low volumes of OPnEO per diagnostic ([redacted][1E-02 – 10 E-02] tonnes OPnEO across <[redacted] [15,000 – 25,000] diagnostics per year) • BD guidance and local legislation result in solid waste for incineration	• Frequency: Daily use by DU (LCS 2). • Guidance on use, disposal and waste characterisation provided to DU by BD • Solid waste to be incinerated	N/A	N/A	• Wastewater emissions: mix of incineration and direct to drain (worst case approach) • Incineration: 100% destruction of the OPnEO. Thus removal of exposure pathway • No emissions to the air; No emissions to the ground	• Water: 30% • Air: no release • Soil: no release	9.2.1 and 9.2.2	CBI 1 & 2

ECS and LCS	Task (ERC / PROC)	Annual amount of OPnEO placed on the UK market (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	Other conditions	Effectiveness of wastewater and waste air treatment (for ERC)	Release factors: water, air and soil (for ERC)	Detailed info. in CSR (section)	
LCS 2 - Use of diagnostics by downstream users	PROC 15	[redacted][1E-02 – 10E-02]	• Diagnostic operation takes place in a laboratory setting • Majority of diagnostic operations using diagnostics take place in closed conditions • There is no cleaning and maintenance of the diagnostics under normal operating conditions	• Daily use by DU across UK. No exposure to OPnEO during operation	PPE requirement dependant on end use	N/A	N/A	N/A	9.2.1 and 9.2.3	CBI 1

Abbreviations: LCS=Life Cycle Stage, ECS=Environmental Contributing Scenario, ERC=Environmental Release Category, PROC= Process category, LEV=Local Exhaust Ventilation, PPE=Personal Protective Equipment

DECLARATION THAT RISK MANAGEMENT MEASURES ARE IMPLEMENTED

The Applicant, Becton, Dickinson U.K. Limited, implements the risk management measures that are discussed in Section 9 of Part B of this document.

DECLARATION THAT RISK MANAGEMENT MEASURES ARE COMMUNICATED

The risk management measures defined in section 9 of part B are communicated to all Becton, Dickinson U.K. Limited employees and customers involved in the processes described in this Chemical Safety Report (CSR).

PART B

9 EXPOSURE ASSESSMENT (AND RELATED RISK CHARACTERISATION)

9.1 INTRODUCTION

4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-OPnEO, 'OPnEO') has been included in Annex XIV to Regulation (EC) No 1907/2006 ('REACH') as it has an equivalent level of concern having probable serious effects to environment (Article 57 f). When UK REACH came into force on 1 January 2021, the UK retained the Authorisation provisions of EU REACH in full.

As noted in the Member State Committee supporting document[1] for the identification of the substance as a SVHC, 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated [4- tert-octylphenol ethoxylates; 4-tert-OPnEO] degrades to 4-(1,1,3,3-tetramethylbutyl)phenol, either in wastewater treatment plants, or via further degradation processes in sediments (e.g. aquatic bodies receiving the wastewater effluents) and soils (e.g. receiving sewage sludge).

OPnEO was identified as a SVHC and placed on the authorisation list of the REACH regulation on 13 June 2017 due to its endocrine disrupting properties with potential serious environmental consequences solely on the basis of the properties of their respective alkylphenol e.g. 4-tert-octylphenol (OP).

Following UK REACH, Article 62(4)(d), the CSR supporting an AfA needs to cover only those potential risks arising from the intrinsic properties specified in Annex XIV. Accordingly, only the endocrine disrupting properties with potential serious environmental consequences related to the use of OPnEO are considered in the current CSR. Potential human health hazard assessment is not required within the scope of this AfA. However, this CSR does detail the use of OPnEO throughout its Life Cycle Stage (LCS). The risk management measures in place at the LCS are documented in the relevant sections of this CSR.

Since OPnEO is a non-threshold substance without a well-defined dose-response relationship, the present risk assessment does not include any calculation of risk characterisation based on a dose-response curve or a PNEC value thereof. The present AfA follows the socio-economic route and the objective of the CSR is to show that emission to the environment has been minimised drastically. Therefore, the focus is set on the residual releases of OPnEO into the environment.

The BD diagnostics are stored in a distribution centre outside the UK and directly shipped to the customers (downstream users (DU)) such as hospitals, blood banks, contract research organisation (CRO) and doctors' surgeries across the UK. As such downstream use is considered as part of the CSR. DU may act as distributors, however there will be no exposure to those DU.

This Chemical Safety Report (CSR), and the associated environmental release category (ERC) and Life Cycle Stage (LCS) supports the Application for Authorisation (AfA) to continue the use of OPnEO as a processing aid in diagnostics imported into the UK by Becton, Dickinson U.K. Limited. and the downstream use of the diagnostics by customers of Becton Dickinson after the sunset date of 30 June 2022.

[1] https://echa.europa.eu/documents/10162/430c2613-588f-8b08-8a72-df4013727ef8

Becton Dickinson does not import OPnEO in any consumer products, therefore exposure for consumers has not been assessed.

The aim of the CSR is to demonstrate that the operational conditions and risk management measures (RMM) in place and detailed in this CSR are appropriate and effective in limiting the risk of OPnEO to the environment.

9.1.1 Overview on uses

Becton Dickinson manufactures a number of diagnostics outside the EEA, primarily in the USA and Canada. These diagnostics are imported into the EEA via their legal entity in Belgium (Becton Dickinson Distribution Center N.V.) and then, from Belgium, directly distributed to UK customers through the legal entity Becton, Dickinson U.K. Limited ('BD').

BD supplies the following types of diagnostics containing OPnEO:

BD Diagnostic	***Placed on the UK market***
BD MAX™	Yes
BD Viper™ LT / BD COR™	Yes
BD Veritor™	Yes
BD Leucocount™	Yes
RUO /LUO	Yes

At the time of submission, the above is an exhaustive list of diagnostics instruments produced by BD for which diagnostics, containing OPnEO, are used. All diagnostic systems listed above are described in section 9.2.1.

In Great Britain (England, Wales and Scotland), devices must conform to the UK Medical Devices Regulation (MDR) 2002, or the EU In Vitro Diagnostic Directive (IVD) in order to be registered with the Medicines and Healthcare products Regulatory Agency (MHRA). For the purpose of this AfA, "diagnostics" means In Vitro Diagnostic Medical Devices (IVD) regulated as per Directive 98/79/EC and similar products (such as for Laboratory Use Only products (LUO) and Research Use Only products (RUO)). LUO and RUO make up very small volumes of the OPnEO placed on the UK market by the applicant and the function of the OPnEO within these products is the same as the other diagnostics mentioned in this AfA.

Becton Dickinson imports into the UK and distributes the diagnostics from their distribution centre outside the UK directly to the DU as required, to hospitals, blood banks CROs, and doctors' surgeries across the UK. Once at these locations the diagnostics are used in the analysis of a number of end points. These end points are summarised below.

- Infectious disease tests (including screening of cancer causing viruses and SARS-CoV-2);
- DNA genotyping & analysis; and
- White blood cell counting in blood products for transfusion.

OPnEO is used within the diagnostics for the solubilisation of hydrophobic proteins and lipids, specifically the lysis of different types of cells where OPnEO is used to disrupt cell membranes (mammalian and bacterial) to release cell contents and maintain protein solubility for subsequent analysis in BD diagnostic systems.

At the end of their life cycle each diagnostic is disposed of as per the national waste legislation in the UK. Section 9.2.1 details the handling and use of all diagnostics placed on the market by BD. The majority of diagnostics are handled in a closed manner with disposal of the diagnostic being the only potential for release of OPnEO to the environment. However, it should be noted that the diagnostic BD Leucocount™ does have some open handling of the reagent and sample during its life cycle. The BD Leucocount™ reagent (that contains OPnEO) is added to the tube containing the blood sample. This addition is carried out via pipette transfer by skilled and trained lab personnel. Even in this case the only potential for release of OPnEO to the environment during normal use of this diagnostic is via the disposal. All contaminated materials, including pipettes, should be discarded in appropriate biohazardous waste containers.

Considering the UK market data for the period 2022–2033, the current risk management measures (RMM) put in place by BD for DU, i.e. the segregation and incineration of solid waste removes 70% (estimated) of all OPnEO placed on the UK market by BD.

BD Viper™ LT /BD COR™, BD Leucocount™ and RUO / LUO diagnostics placed on the UK market by BD generate in addition to solid waste, which is subject of incineration, small amounts of OPnEO containing liquid waste (estimated to be 30% of all OPnEO placed on the UK market by BD). BD guidance for BD Viper™ LT / BD COR™ stated that this liquid waste is to be neutralised, treated with bleach and discharged to the drain and for BD Leucocount™ and RUO / LUO it is stated that this liquid is to be treated with bleach and handled according to local regulations. BD will start to instruct customers, as outlined in Section 9.2.1, to dispose of liquid waste differently. Nevertheless, taking a transitional period into account, BD has taken the worst-case scenario for this AfA and assumed all liquid waste is released to the environment. As this discharge is spread across the whole of the UK and it cannot be confirmed where the end point of liquid waste is, i.e. incineration, municipal wastewater treatment plants (WWTP), on-site WWTP, directly to river, the environmental fate of OPnEO was not taken into account and the worst-case scenario was assumed (whereby all OPnEO release breaks down to OP). This approach is detailed in later sections of this CSR. Based on the mass reduction from OPnEO to OP (see Table 9-2) the maximum estimated amount of OP released that can be attributed to BD is [redacted] [1 – 10] kg OP/year across the entire UK.

CBI 1

There is no cleaning and maintenance of the diagnostics under normal operating conditions.

9.1.2 Information on use applied for (use descriptor system)

Life cycle stage (LCS)	PROC 15 (Use of diagnostics in diagnostic systems by downstream users)
Sector of Use (SU)	SU 20 (Health Services), SU 24 (Scientific research and development)
Product Category (PC)	PC 21 (Laboratory Chemicals)
Environmental Release Category (ERC)	ERC 8a (Used as a processing aid in imported diagnostics for diagnostic systems)
Technical Function Category (TF)	Surfactant

9.1.3 Introduction to the assessment for the environment

9.1.3.1 Tonnage

All diagnostics are imported from Becton Dickinson Distribution Center N.V. and then distributed by BD UK sales to hospitals, CRO's and doctors' surgeries across the UK.

The estimated maximum amount of diagnostics placed on the UK market per year for the requested review period is about [redacted] [15,000 – 25,000], corresponding to [redacted] [10-100] kg OPnEO. CBI 2

This data does not take into account any diagnostics containing < 0.1% (w/w) OPnEO as, at this final concentration in mixtures, the substance is out of the scope of authorisation.

Table 9-1 provides the tonnage per use and environmental contributing activity.

Table 9-1 Tonnage for assessment

ES#	Exposure scenario (ES) name and related environmental contributing scenarios	Tonnage OPnEO per use (t/year)	Daily tonnage OPnEO (t/day)
ES1	Used as a processing aid in imported diagnostics for diagnostic systems by downstream users (ERC 8a)	[redacted] [1 E-02 – 10 E-02]	[redacted] [2.7 E-05 – 2.7 E-04]

CBI 1

Assessed tonnage / year: [redacted] [0.01 – 0.10] tonnes/year (maximum amount expected for the requested review period).

CBI 1

Assessed tonnage / day: [redacted] [0.027 - 0.27] kg/day, calculated using the following equation:

$$Daily\ tonnage\ = (Annual\ Tonnage)\ \div 365\ (Days\ per\ year)$$

9.1.3.2 Scope and type of assessment for the environment

OPnEO is a SVHC because of potential serious environmental consequences as a result of the endocrine disrupting properties of its breakdown products.

9.1.3.3 Fate and distribution parameters

Physicochemical properties used for exposure estimation

The following are the key substance properties for OPnEO and OP.

Table 9-2 Substance key phys-chem and fate properties

Substance property	Value (OPnEO)	Value (OP)
Molecular weight used for the assessment	646 g/mol	206 g/mol
Melting point at 101 325 Pa	6 °C	44 °C
Vapour pressure	0.01 hPa at 20 °C	0.02 hPa at 20 °C
Partition coefficient (Log Kow)	3.49 at 20 °C	4.8 at 22 °C
Water solubility	3.73 mg/L at 20 °C	7 mg/L

9.1.3.4 Comments on assessment approach for the environment

When assessing OPnEO that may be released into the environment the biodegradation behaviour needs to be assessed. OPnEO, and alkylphenol ethoxylates in general, degrade in a complex manner within the environment[2]. The step degradation process is shown in Figure 9-1 with a more detailed version provided in the Member State Committee support document for identification of 4-(1,1,3,3-Tetramethylbutyl)Phenol, Ethoxylated as a SVHC[3]. Based on the molecular structures the molecular weight of OPnEO (646 g/mol) is 3.14 times greater than that of OP (206 g/mol based of the formula $C_{14}H_{22}O$). Therefore, the total mass of emissions of OP to the environment will be 3.14 times lower than the OPnEO emitted.

However, if OPnEO in liquid waste from diagnostics is released it is expected that this will be via a municipal sewer system and not directly into a water course. As such the fate of OPnEO within biological wastewater treatment plants (WWTP) need to be assessed, as this is by the far the most common treatment of sewer water. The below figure shows a

[2] https://www.semanticscholar.org/paper/Behaviour-of-alkylphenol-polyethoxylate-surfactants-Ahel-Giger/4de2131cc4faeb267efd448f163ac818d64744e2

[3] https://echa.europa.eu/documents/10162/dfc9c8c4-8b13-1ed8-a066-1486d2b7427e

stepped degradation progression that ends in the alkyl phenol, however the reality is that in a WWTP not all of the alkylphenol ethoxylate is degraded to the alkyl phenol. For example, the carboxylic acids shown below are more resistant to biodegradation than the alkylphenol ethoxylates. Ahel[4], noted that nonylphenol ethyoxylate (NPnEO) degraded to several metabolites, with nonylphenol accounting for a total of 25% of the original NPnEO (corrected for molecular weight). In addition, 90% of this 25% was adsorbed onto digested sludge due to the lipophilic nature of nonylphenol (NP), therefore resulting in just 2.5% of the original NPnEO being released as NP in the effluent of sewage treatment plants.

OPnEO is structurally very similar to NPnEO with just one methyl group difference. It is therefore highly likely that similar levels of OP, to those of NP, would be observed in effluent. Additionally, the molecular weight correction factors are very similar. Therefore, it can be concluded that approximately 2.5% of OPnEO would be released as OP in effluent.

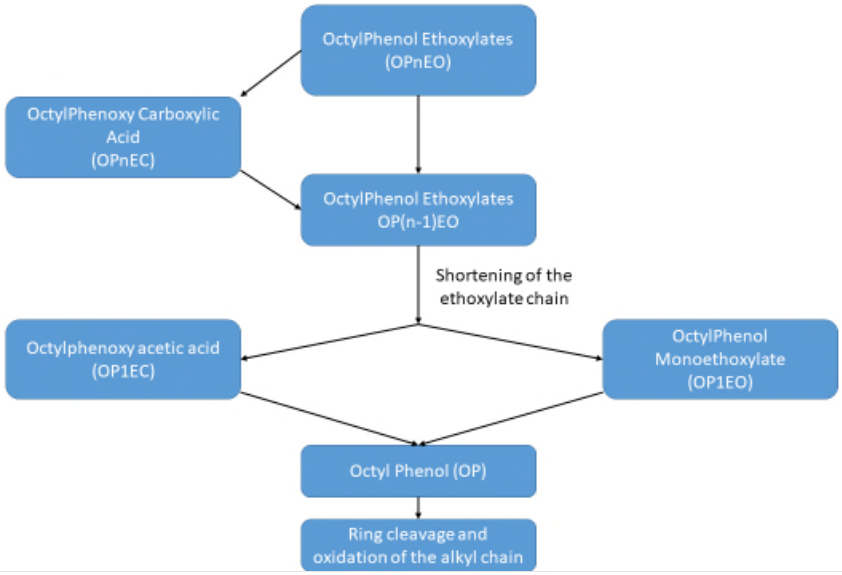


Figure 9-1 Biodegradation pathway for alkylphenol ethoxylates

There is no PNEC available for OP, however, Directive 2008/105/EC on environmental quality standards in the field of water policy does provide an environmental quality standard (EQS) for Octylphenol ((4-(1,1',3,3'-tetramethylbutyl)- phenol)) of 1.0 E-4 mg/L[5]. This is aligned with the EQS proposed by UK Authority in 1999[6].

9.1.3.5 Scope and type of assessment for man via environment

The dominating effect resulting from the intrinsic hazardous properties of OPnEO is the potential serious environmental consequences as a result of its endocrine disrupting

[4] https://www.semanticscholar.org/paper/Behaviour-of-alkylphenol-polyethoxylate-surfactants-Ahel-Giger/4de2131cc4faeb267efd448f163ac818d64744e2

[5] https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:348:0084:0097:EN:PDF

[6] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/183101/nonylphenol_rrs.pdf

properties. As such the assessment of man via the environment is not relevant and evaluation of any potential hazard to human health via this route is not required within the framework of this AfA.

9.1.4 Introduction to the assessment for workers

9.1.4.1 Scope and type of assessment for workers

The dominating effect resulting from the intrinsic hazardous properties of OPnEO is the potential serious environmental consequences as a result of its endocrine disrupting properties. As such uses by workers in professional settings are not relevant and evaluation of any potential hazard to human health is not required within the framework of this AfA.

However, the control measures BD put in place, via documentation provided to their downstream users have been detailed in the sections below.

General information on risk management related to toxicological hazard:

The diagnostics are shipped to the UK and directly delivered to the customers (downstream users). Each diagnostic is shipped with a technical data sheet and/or user manual that outlines the engineering and administrative control measures that should be in place alongside the PPE that should be used when using the diagnostics. A full description of how the diagnostics are used and then disposed of is provided in Section 9.2.3.

9.1.5 Introduction to the assessment for consumers

Exposure assessment is not applicable as there are no consumer-related uses for the substance.

9.2 EXPOSURE SCENARIO 1: WIDESPREAD USE BY PROFESSIONAL WORKERS - USE OF 4-(1,1,3,3-TETRAMETHYLBUTYL)PHENOL, ETHOXYLATED (4-TERT-OPNEO)) AS A PROCESSING AID IN IMPORTED DIAGNOSTICS.

Product category used: PC 21: Laboratory Chemicals

Sector of use: SU 20: Health services; SU 24: Scientific research and development

Environment contributing scenario(s):		
ECS 1	Used as a processing aid in imported diagnostics	ERC 8a
Worker/consumer contributing scenario(s):		
not applicable		
Life Cycle Stage(s):		
LCS 2	Use of diagnostics by downstream users	PROC 15

9.2.1 Further description of the use

9.2.1.1 Downstream User Uses

Each diagnostic system works in broadly the same manner, in that they are constituted of:

- **A diagnostic instrument (an analytical system)** – this is the overall body of the diagnostic system and is used to load and house the diagnostic during analysis.
- **A diagnostic** – contains test cassettes or cartridges or reagents compatible for a specific instrument. The reagents present in the diagnostic are specifically formulated for the target analyte which constitute the test. Therefore, the contents of specific reagents will vary dependent on the test being run. For example, a BD MAX™ diagnostic testing for pathogens responsible for enteric diseases will have a different reagent mix to a BD MAX™ diagnostic testing for pathogens responsible for sexually transmitted infections (STI).

Further details of the types of diagnostics are given below, providing explanations of use, disposal and potential for environmental discharge of OPnEO.

BD MAX™

The figures below illustrate the overall BD MAX™ instrument (Figure 9-2), and a breakdown of the key components (Figure 9-3) of the disposable diagnostic. The blue front of the analytical system in Figure 9-2 can be opened and closed and it is into this that the diagnostic is loaded. The front is then closed and is not opened again until the analysis has been completed. The results of the analysis are displayed on the screen shown. This kit is likely to be used at hospitals and / or laboratories.

Each diagnostic (named "box" in Figure 9.8) includes 24 tests and all required reagents (unitized reagent strips, extraction reagent tubes, master mixes, sample buffer tubes, septum caps). The diagnostic is used to detect particular pathogens. There is the option to mix and match the tests present in the diagnostic, e.g. a diagnostic could be used to detect enteric pathogens, mycobacterium tuberculosis etc. The instrument will read the barcode present on all reagent and will determine the test to be run, ensure the correct reagents are present, and what volume to use from the patient sample.

The BD MAX™ analytical system can operate a number of different tests at the same time. The workflow for the process of all BD MAX™ diagnostics is similar and outlined in the procedure below.

- A sample specimen is collected and transported to the laboratory – the sample is then transferred to the Sample Buffer Tube (Figure 9-6). The Sample Buffer Tube (SBT) is closed with a septum cap or a pierceable cap.
- The unitized reagent strip, including the snapped in extraction and master mix tubes, along with the BD MAX™ cartridge (Figure 9-6) and SBT are loaded on the BD MAX™ System and a worklist is created via the software in the analytical system. The BD MAX™ System automates sample preparation, DNA extraction amplification and detection. This automated procedure runs in a closed system and no further operator intervention is required.
- OPnEO is generally found in the sample buffer tube but it can also be found in the wash buffer, extraction tube or master mix tube depending on the test being run by the BD MAX™ system.

- All of these tubes containing reagents, including OPnEO, are filled during the manufacture of the diagnostics in the USA or Canada. These tubes are then sealed prior to shipment.
- During normal operation once all the reagents are loaded into the analytical system there is no human interaction and the analysis and results interpretation are run automatically. There is no manual removal of seals or packaging when loading the diagnostics.
- At the end of the process, the final reaction in the PCR cartridges will be sealed by the system in the BD MAX™ instrument to prevent evaporation and any cross contamination.
- The used sealed PCR cartridges are then suitable for disposal (see below). There is no liquid waste produced from BD MAX™ systems.

The technical documentation that is supplied with the BD MAX™ System also outlines warnings and precautions when using the diagnostic. Whilst a number of these are related to the use of the diagnostic and ensuring reliable and repeatable results, the following are given with regards to disposal of the finished cartridges and other consumables:

- Do not use the diagnostic if the label that seals the outer box is broken upon arrival.
- Do not use reagents if the protective pouches are open or broken upon arrival.
- Do not use reagents if the foil has been broken or damaged.
- Do not mix reagents from different pouches and/or diagnostics and/or lots.
- Good laboratory technique is essential to the proper performance of the tests.
- To avoid contamination of the environment do not break apart the BD MAX™ cartridges after use. The seals of the cartridges are designed to prevent contamination.
- Always handle specimens as if they are infectious and in accordance with safe laboratory procedures such as those described in the Clinical and Laboratory Standards Institute: Protection of laboratory workers from occupationally acquired infections (Document M29) and in Centres for Disease Control and Prevention, and National Institutes of Health[7].
- Wear protective clothing and disposable gloves and wash hands thoroughly after performing the test.
- Do not smoke, drink, chew or eat in areas where specimens or diagnostic reagents are being handled.
- Dispose of unused reagents and waste in accordance with local, state, provincial and/or federal regulations.

Similar guidance and warnings to the ones mentioned above are included in either the user manual, instructions for use and/or safety data sheets of impacted BD diagnostics. This guidance includes that all specimens should be handled as if they are infectious and disposed of per local regulations.

In addition, BD will be including the following instructions in the product documentation and/or the Instructions for Use (IFU):

Collect and dispose of all used and unused reagents and any other contaminated disposable materials following procedures for biohazardous or potentially biohazardous waste. It is the responsibility of each laboratory to handle solid and liquid waste according to their nature and degree of hazardousness and to adequately treat and dispose of them

[7] https://www.cdc.gov/labs/pdf/SF__19_308133-A_BMBL6_00-BOOK-WEB-final-3.pdf

(or have them treated and disposed of) in accordance with any applicable regulations. Do not discharge liquid waste down the drain where prohibited.

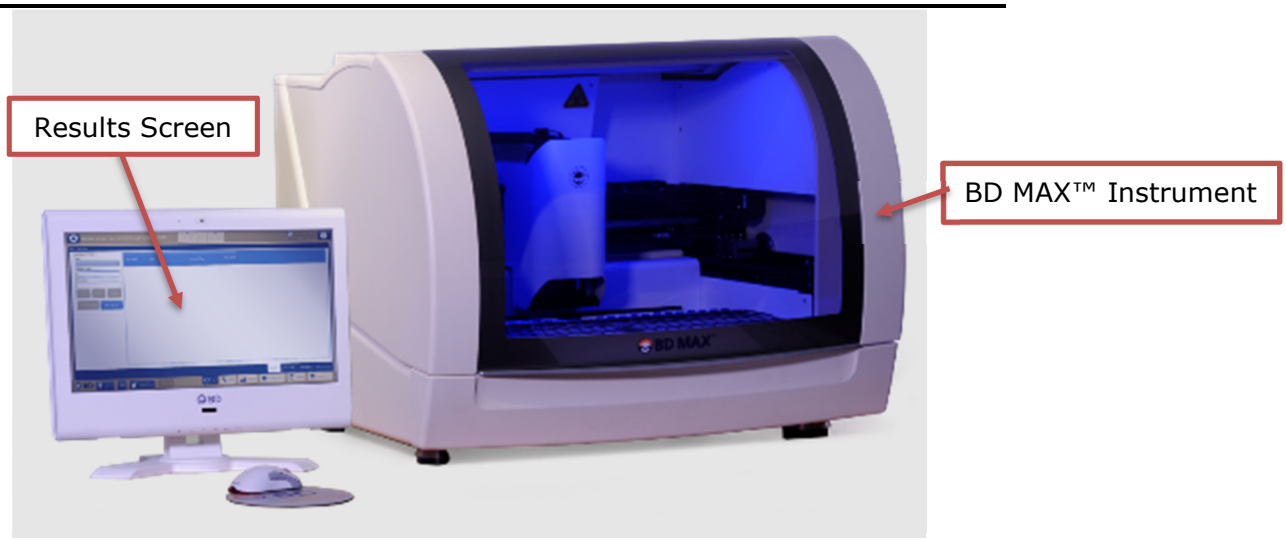
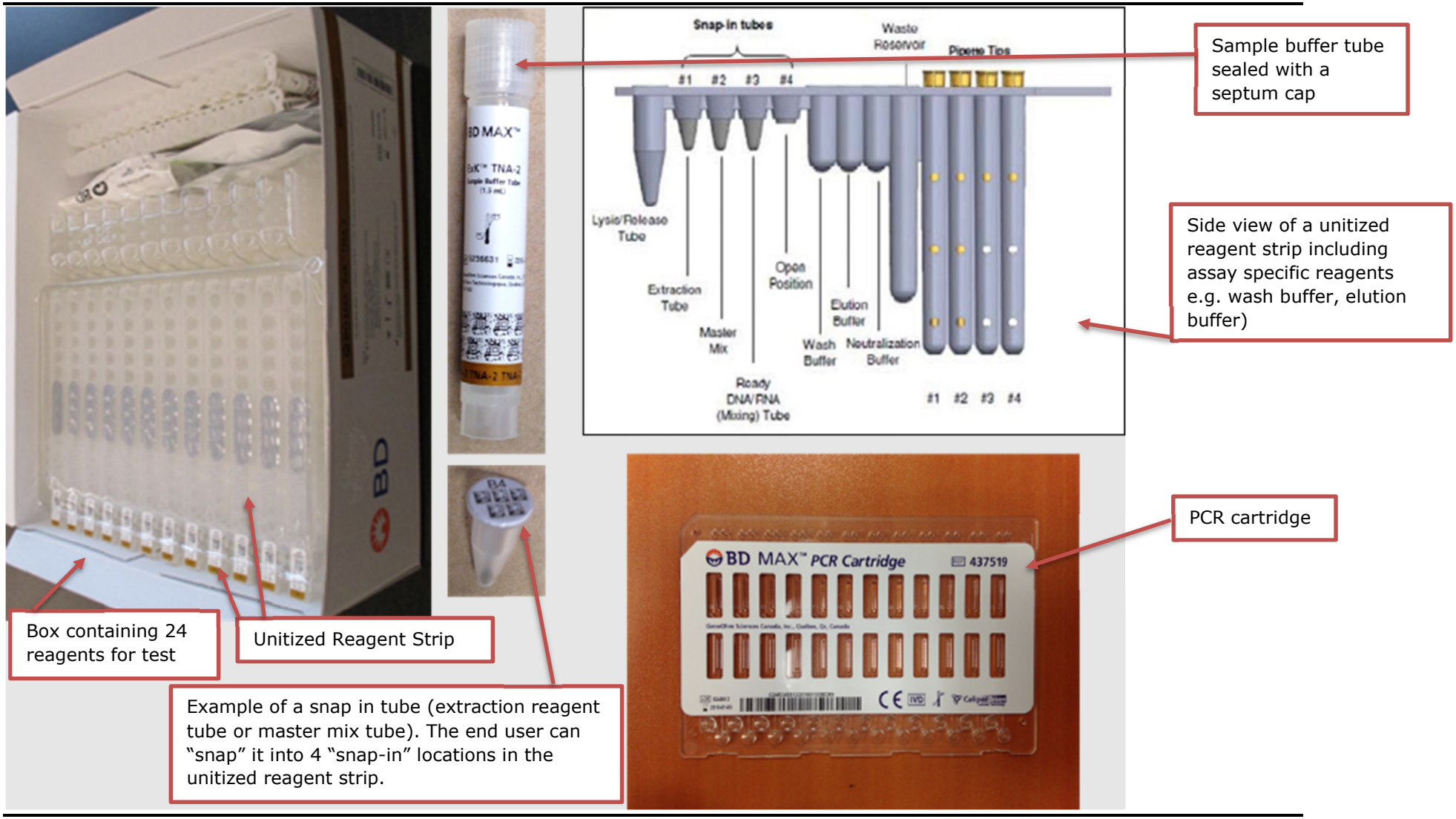


Figure 9-2 BD MAX™ Instrument

Figure 9-3 Breakdown of BD MAX™ Diagnostic



BD Viper™ LT

The BD Viper™ LT system is operated in a similar manner to the BD MAX™ system described above. The main difference is that the BD Viper™ LT system has a higher throughput as it operates a greater batch size. BD Viper™ LT may also require manual handling if the user needs to express the swab/brush or pipette the sample into the sample tube. However, the control mechanisms outlined above, including the disposal considerations and operation as a closed system with no exposure or emissions of OPnEO under normal conditions, are the same.

Unlike BD MAX™ instrument, liquid waste is generated by the BD Viper™ LT instrument, as residue of the of DNA extraction, including OPnEO. This liquid waste is automatically segregated in a separate sealed liquid waste container within the instrument. This liquid waste does contain the sample, along with other chemical solutions used in the automated processing of the sample, so it is classified as biohazardous. OPnEO is present in the liquid waste.

BD guidance was for the pH of the liquid waste to be neutralised using a neutralization pouch. The neutralized liquid waste could then be treated with bleach to render non biohazardous before disposal via either a chemical sink or to the drain.

However, BD has recently changed disposal instructions in the user manual of BD Viper™ LT instrument to the following:

Dispose the contents of the waste container in accordance with applicable regulations. Do not discharge the liquid waste down the drain where prohibited.

In addition, BD will be including the following instructions in the product documentation and/or the Instructions for Use (IFU):

Collect and dispose of all used and unused reagents and any other contaminated disposable materials following procedures for biohazardous or potentially biohazardous waste. It is the responsibility of each laboratory to handle solid and liquid waste according to their nature and degree of hazardousness and to adequately treat and dispose of them (or have them treated and disposed of) in accordance with any applicable regulations. Do not discharge liquid waste down the drain where prohibited.

Figure 9-4 shows the BD Viper™ LT instrument and Figure 9-5 details the BD Viper™ LT workflow, specifically for the BD Viper™ LT diagnostic.

Figure 9-4 BD Viper™ LT Instrument

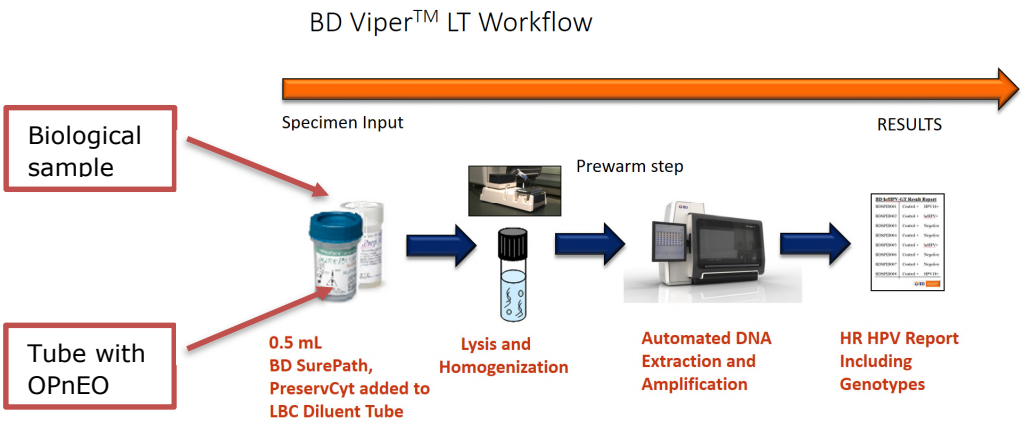


Figure 9-5 BD Viper™ LT Workflow

BD COR™

BD COR™ System is a fully automated, modular, sample preparation/PCR system that will address the Core and Reference Labs' fundamental needs to improve workflow efficiency, control costs, and provide differentiated, clinically relevant results. A flexible layout and broad test menu will allow the end user to focus on the most relevant tests for their patient population.

The BD COR™ System is a high-volume test and comprises three individual modules, PX (preanalytical module), GX (HPV analytical module) and MX (molecular diagnostics analytical module) (FIGURE 9-6), that are configured to allow the testing needs of the user. The modules can be installed in multiple configurations and do not function as standalone units. The center module (PX) is required for all installations (pre-analytical workflow), while the BD COR™ Analyzers (GX and MX) can be interchanged in various configurations to make up a BD COR™ System that satisfies individual customer needs.

- The pre-analytical module (PX) manages all processing and analysis logistics for up to 2000 patient samples per day.
- The GX module is designed to perform the BD Onclarity™ HPV Test using the core technology found in the BD Viper™ LT instrument (this system is described in a separate section above).
- The GX is fundamentally designed to be a larger capacity BD Viper™ LT system, therefore, preserving to the greatest extent possible the technical functionality employed by the BD Viper™ LT. While the GX is processing samples, consumables can be loaded and reloaded, allowing for higher throughput and more user flexibility compared to the BD Viper™ LT.
- The MX module is designed to perform the tests that are currently processed on the BD MAX™ (this system is described in a separate section above). The MX module will use the core technology found in the BD MAX™ instrument, including consumable and hardware design elements. The MX instrument is fundamentally designed to be a larger capacity BD MAX™ system, preserving to the greatest extent possible the technical functionality employed by the BD MAX™. While the formulations remain the same, the MX reagent containers and consumables differ from those on BD MAX™ to allow for loading of reagents and consumables for processing multiple batches of samples and reloading of the consumables while the instrument is processing samples.

All reagents and consumables required for the BD COR™ System are delivered in a ready to load format.

The whole process takes place fully automated in a closed system (including e.g. sample sorting, vortexing, uncapping, aliquoting, recapping). Internal cameras monitor the internal processes.

Figure 9-6 BD COR™ Instrument Configuration with the three modules PX, GX and MX

Depending on the analyser being used there is the potential for the BD COR™ instrument to have liquid waste that contains OPnEO, as per the BD Viper™ LT instrument. From BD

guidance the liquid waste could be neutralized (adding a neutralization pouch), treated with bleach and poured down the drain. OPnEO is present in the liquid waste. However, BD has recently changed disposal instructions in the user manual of the BD COR™ instrument to the following: *Dispose the contents of the waste container in accordance with applicable regulations. Do not discharge the liquid waste down the drain where prohibited.*

In addition, BD will be including the following instructions in the product documentation and/or the Instructions for Use (IFU):

Collect and dispose of all used and unused reagents and any other contaminated disposable materials following procedures for biohazardous or potentially biohazardous waste. It is the responsibility of each laboratory to handle solid and liquid waste according to their nature and degree of hazardousness and to adequately treat and dispose of them (or have them treated and disposed of) in accordance with any applicable regulations. Do not discharge liquid waste down the drain where prohibited.

OPnEO present in the liquid waste is further examined in the section on waste below.

BD Leucocount™

The BD Leucocount™ kit is designed for counting residual white blood cells in leucoreduced blood products. This counting is done via the utilisation of a flow cytometer. The components of the diagnostic are the BD Leucocount™ reagent and BD Trucount™ tubes (see Figure 9-7) and the process workflow is shown in Figure 9-8.

This product is available in UK for use on cytometers, such as BD FACSVia™ system (Figure 9-9) and the BD FACSCalibur™ flow cytometer (Figure 9-10).

When the workflow (Figure 9-8) has been completed the waste reagent is treated as per UK waste regulations (see Section 9.2.1.3). The same statement applies to any uncleaned or contaminated packaging, as well as equipment that has been used and may be contaminated (e.g. pipettes used for transfer of reagent). It is noted on the safety data sheet to avoid release to the environment.

As with BD Viper™ LT there is a very small amount of liquid waste generated during the operation of BD Leucocount™. From BD guidance the liquid waste was treated with bleach and could then be disposed of in the same manner as BD Viper™ LT and BD COR™. No neutralisation step was required for this product group. However, BD is changing its guidance and the following instructions will be included in the technical documentation:

Collect and dispose of all used and unused reagents and any other contaminated disposable materials following procedures for biohazardous or potentially biohazardous waste. It is the responsibility of each laboratory to handle solid and liquid waste according to their nature and degree of hazardousness and to adequately treat and dispose of them (or have them treated and disposed of) in accordance with any applicable regulations. Do not discharge liquid waste down the drain where prohibited.

OPnEO present in the liquid waste is further examined in the section on waste below.

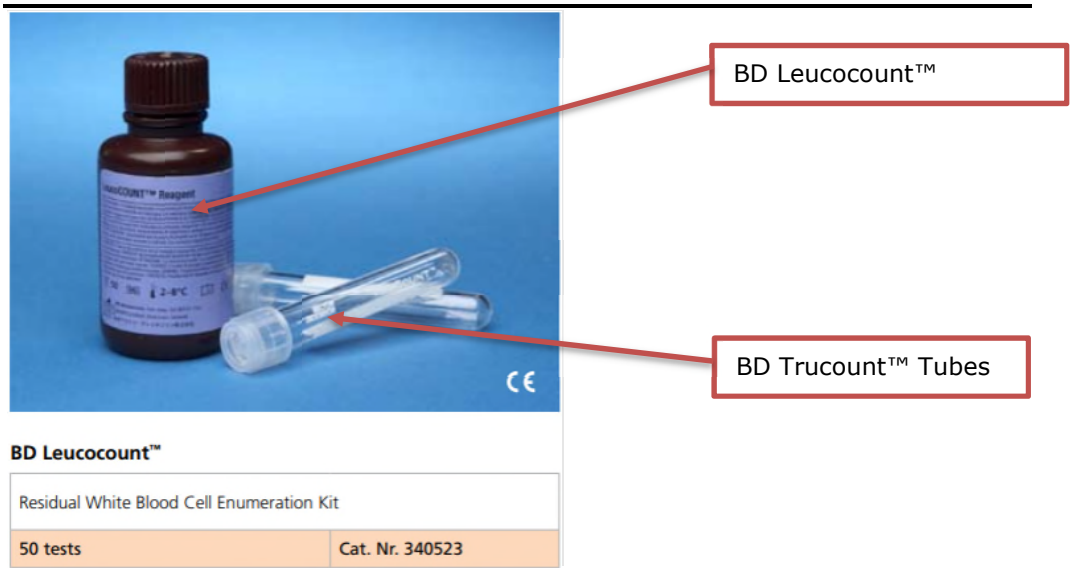


Figure 9-7 BD Leucocount™ Components

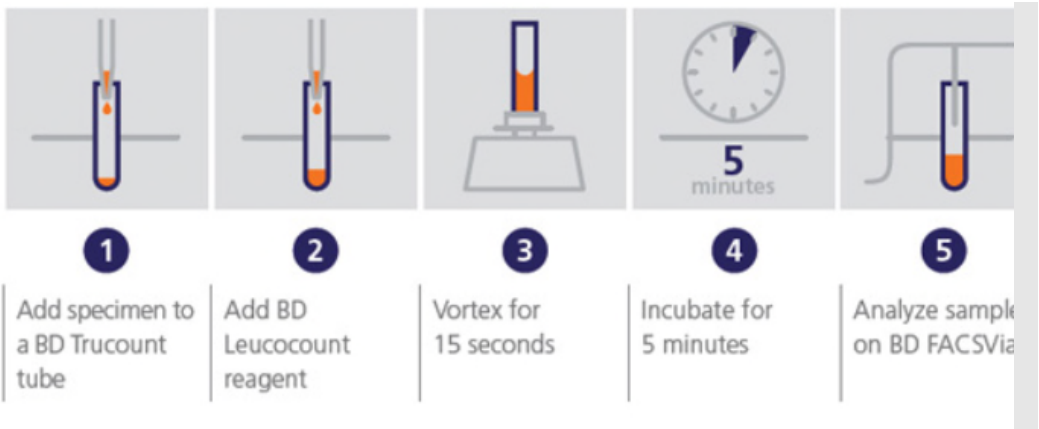


Figure 9-8 BD Leucocount™ Workflow

Figure 9-9 BD FACSVia™ Flow Cytometry system

BD FACSCalibur Flow Cytometry System ...

Figure 9-10 BD FACSCalibur™ flow cytometer

BD Veritor™

The BD Veritor™ system (Figure 9-11) is a CE-marked line of digital immunoassay products, used in in healthcare settings that include primary-care physician offices, retail clinics, retail pharmacies, urgent-care facilities, and acute-care settings. The system is currently used to aid in the diagnosis of influenza A and B, respiratory syncytial virus (RSV), and Group A Streptococcus. For each of these tests, the system delivers lab-quality test results at the point of care within minutes.

As with other diagnostics systems, BD Veritor™ is operated as a closed system with no exposure or emissions of OPnEO under normal conditions. During use there is a transfer of OPnEO containing solution, however there is no pipette use (like the BD Leucocount™ diagnostics). The transfer amount and speed is controlled by a cap that limits the amount of the OPnEO containing solution that is transferred onto a diagnostic strip to three drops. This transfer is carried out by a professional or trained user. The sample tube and control cap are to be disposed of as biohazardous waste.

Figure 9-11 BD Veritor™

BD will be including the following instructions in the product documentation and/or the Instructions for Use (IFU):

Collect and dispose of all used and unused reagents and any other contaminated disposable materials following procedures for biohazardous or potentially biohazardous waste. It is the responsibility of each laboratory to handle solid and liquid waste according

to their nature and degree of hazardousness and to adequately treat and dispose of them (or have them treated and disposed of) in accordance with any applicable regulations. Do not discharge liquid waste down the drain where prohibited.

Laboratory Use Only (LUO) and Research Use Only (RUO)

OPnEO is present in buffer solutions in BD tests that are used for laboratory purpose or in a R&D environment. The OPnEO present in these LUO and RUO diagnostics is used in cell lysis, i.e. the same use as OPnEO in the diagostics listed above. However, BD LUO and RUO diagnostics are not to be used in clinical diagnosis. LUO and RUO make up a very small volumes of the OpnEO placed on the UK market by BD. No specific instructions are currently provided, but LUO and RUO are used by professional or trained users in laboratory settings and similar guidance will be provided as for the diagnostics above.

9.2.1.2 Cleaning and Maintenance

As the above process descriptions show there is no in-situ cleaning or maintenance of the diagnostics at downstream user facilities. The analysis of the sample, and therefore any use of OPnEO contained in individual solutions that are part of the diagnostic, takes place in a closed system – the test cartridge.

9.2.1.3 Waste Generated through the use of diagnostics

The diagnostics placed on the market generate solid and liquid waste, with each waste stream being handled in a different manner (as outlined above). The following table provides the estimated breakdown of total solid waste vs. total liquid waste produced from the approximate [redacted] [10,000 – 25,000] diagnostics (diagnostic instruments outlined above) expected to be placed on the UK market annually. The share of liquid and solid waste is expected to remain the same during the requested review period (2022-2033).

CBI 2

Table 9-3 Estimated amount of OPnEO and Solid vs Liquid waste (per year)

Diagnostic	Amount of OPnEO (Kg)	Amount of OPnEO (Kg) and % in solid waste	Amount of OPnEO (Kg) and % in liquid waste
Total	[redacted] [10-100]	[redacted] [7-70] 70%*	[redacted] [3-30] 30%*

CBI 1

*waste percentages are estimated using projected sales figures of all BD diagnostics.

The used diagnostics and any unused reagents are treated as waste and BD's guidance to customers is that waste from diagnostics is to be disposed of in accordance with local, state, provincial and/or federal regulations.

BD state in their technical documentation that users should *"always handle specimens as if they are infectious and in accordance with safe laboratory procedures".* By stating that the specimens are infectious then the solid waste generated is thus classified in the UK as biohazardous waste. The definition of biohazardous waste includes:

- Human blood and its components, in liquid or semi-liquid form, dried or not
- Human bodily fluids in liquid or semi-liquid form, dried or not
- Human pathological waste: all human tissues, organs, and body parts

The European Waste Catalogue (EWC) codes are used for the classification of all wastes and hazardous wastes and are designed to form a consistent waste classification system across the UK[8],[9]. As noted above, the diagnostic waste is biohazardous as the specimen should be treated as infectious. Using the EWC codes this waste is classified as follows:

- Code 18 - wastes from human or animal health care and/or related research (except kitchen and restaurant wastes not arising from immediate health care)
- Category: 18 01 - wastes from natal care, diagnosis, treatment or prevention of disease in humans
- Sub-category: 18 01 03* - wastes whose collection and disposal is subject to special requirements in order to prevent infection. Under the EWC Codes any waste marked with an asterisk (*) is considered as a hazardous waste and would thus be disposed as directed by individual country legislation.

Hazardous Waste (England and Wales) Regulations (as last amended in 2020[10] by the European Waste Framework Directive - WFD) require that waste streams are safely disposed, and that waste management is carried out without endangering human health or harming the environment. Regarding the sanitary waste stream, which includes the code 18 01 03*, there are two processes most often used in the treatment of hazardous waste: incineration and sterilisation (autoclaving). Incineration is considered the safest, most effective means of treatment of biohazardous waste as the waste is completely destroyed and is unrecognisable in make-up, as would be the case of BD diagnostics. The table below outlines how waste categorised 18 01 03* is disposed of in each of the countries BD ship their diagnostics to. Incineration is a very effective treatment of OPnEO. In the controlled conditions of an incinerator OPnEO will be oxidised to carbon dioxide.

The Table 9-4 below shows that if BD customers follow national waste legislation then there should be no release of OPnEO to the UK environment from solid waste.

Table 9-4 National Waste Disposal Methods for EWC 18 01 03

Country	Disposal technique of biohazardous waste per country	Comment	Total amount of OPnEO released to the environment (kg)
United Kingdom	Incineration	The Department of Health (2013) states that infectious waste from human healthcare with an EWC code of 18 01 03 must be disposed of using clinical waste incineration only	**0.0**

8 https://www.ciwm.co.uk/Custom/BSIDocumentSelector/Pages/DocumentViewer.aspx?id=QoR7FzWBtisamYEcWSfL6SxAJRLAPT9vl3Da9d0xu%252fXTw5Mn4fZYAs61fy8XU42G3dW3Woc%252fqkFfz79Mdq%252bx0PL0ZaeQVXQpjMNCJ6I7%252bAZX5z7moORcwDssj372vi17zLkGZ44Eef3A5QLiIA5GdA%253d%253d

9 https://www.england.nhs.uk/wp-content/uploads/2021/05/HTM_07-01_Final.pdf

10 https://www.legislation.gov.uk/uksi/2020/904/contents/made

As outlined above, an estimated 30% of the OPnEO in BD diagnostics is expected to be present in liquid waste in the short to medium term based on BD projected forecasts. There is the potential for this waste stream to be discharged to the environment and not handled as per Table 9-4.

9.2.2 Env. CS 1: Used as a processing aid in imported diagnostics (ERC 8a)

All OPnEO present in the solid waste generated by the diagnostics supplied to the market by BD is contained and disposed of as biohazardous waste. Table 9-4 details how biohazardous waste is disposed of and thus how much OPnEO used in BD diagnostics is released to the environment in the UK.

By adopting a worst-case scenario, BD has approached the assessment as there is the potential for OPnEO present in liquid waste to be released to the environment.

Table 9-5 ECS 1: Conditions of Use

Amount used, frequency and duration of use (or from service life)
• Daily regional (UK wide) widespread use amount: <= [redacted] [0.027 – 0.27] kg OPnEO / day (Table 9-1). *Daily use by hospitals, CRO's, doctors across the EEA*
Conditions and measures related to biological sewage treatment plant
• Biological STP: not known *As previously stated during the storage and use of the BD diagnostics there is no release of OPnEO to the sewer. As such the type of sewage treatment plants present at the BD distribution centre is not relevant. Due to the very diverse number of DUs it is not possible to determine how wastewater released from these locations is treated. However, it is fair to assume that the majority will be treated by either on-site or municipal WWTP.*
Conditions and measures related to external treatment of waste (including article waste)
• Particular considerations on the waste treatment operations –. Solid *waste generated by the use of the BD diagnostics that contain OPnEO is classified as EWC Code 18 01 03* and thus hazardous. BD state that this waste should be disposed of in accordance with local, state, provincial, and/or federal regulations.Incineration of the used diagnostics leads to no release of OPnEO into the environment.*
Other conditions affecting environmental exposure
• Place of use: Indoor

CBI 1

9.2.2.1 Releases

The local releases to the environment are reported in the following table. As noted earlier in this document under normal operating conditions there should be no emissions of OPnEO to the environment.

Table 9-6 Releases to the environment

Release	Release estimation method	Explanations
Water	Estimated release factor	Release factor: 30% Release rate (UK Wide): [redacted][3 - 30] kg OPnEO/year Release rate (UK wide): [redacted][1 - 10] kg OP/year Explanation: see statements on waste management
Air	Estimated release factor	Release factor: 0% Explanation: see statements on waste management
Non-agricultural soil	Estimated release factor	Release factor: 0% Explanation: see statements on waste management

CBI 1

9.2.2.2 Risk characterisation (minimisation of emission/exposure)

Due to the wide dispersive use of BD diagnostics across the UK it has not been possible to determine a risk characterisation ratio (RCR).

9.2.3 LCS 2: Use of diagnostics by downstream users (PROC 15)

Diagnostic operation will take place in a laboratory setting, either within a contract research organisation (CRO); a hospital, and / or a doctor's surgery.

Section 9.2.1details:

- The operating conditions for each type of diagnostic;
- The control mechanisms surrounding disposal of the diagnostics; and
- The reasons why there is no requirement for downstream users to clean or maintain diagnostics containing OPnEO.

Table 9-7 LCS 2: Conditions of Use

Product (Article) Characteristics
• Percentage (w/w) of substance in mixture/article: [redacted] [4 - 7] % This is the maximum concentration of OPnEO found in BD diagnostics.
• Physical form of the used product: Liquid
Amount used (or contained in articles), frequency and duration of use/exposure
• Duration of activity: <= 8.0 h/day. The diagnostics and analytical systems will be used in a lab setting but as noted above there is no potential for environmental exposure of OPnEO during normal operating conditions.
Technical and organisational conditions and measures
• General ventilation: Basic general ventilation (1-3 air changes per hour)
• Occupational Health and Safety Management System: Advanced
• Local exhaust ventilation: No
Conditions and measures related to personal protection, hygiene and health evaluation
• Respiratory protection: No
• Dermal protection: No
Other conditions affecting workers exposure
• Place of use: Indoor
• Operating temperature: <= 20.0 °C

CBI 1

9.2.3.1 Exposure and risks for workers

As the dominating effect resulting from the intrinsic hazardous properties of OPnEO is the potential serious environmental consequences as a result of the endocrine disrupting properties of the break down products, there is no available DNEL. As such no risk characterisation ratio (RCR) can be derived from these exposure estimations.

9.2.4 Measures planned for monitoring and controlling emissions in the review period

In the previous application for EU REACH, a customer survey was conducted related to waste handling. From the cohort surveyed (n=31) it could be confidently concluded that 100% of solid waste and 93% of unused solid waste is disposed through incineration or use of private/national contractors. For UK there was one response, that due to capacity issues for incineration unused material is autoclaved. For liquid waste there was more variability by country with provision to dispose by incineration where decontaminated waste is disposed into the drain, incinerated, or removed by private and national contractors. Only three out of the 28 customers from which it was able to get clear responses indicated that they direct liquid waste down the drain.

As outlined in Section 9.2.1 BD has developed new guidance which will apply to all liquid waste produced by BD diagnostics that contain OPnEO. The implementation of this new guidance will be finalised by early 2023. It directs downstream users to collect and dispose of liquid waste that contain OPnEO via adequate treatment methods that limits the possibility of OPnEO entering the environment. This aligns with the responses regarding liquid waste from the customer survey in the EU application, although the majority of respondents confirmed that their liquid waste treatment does remove the pathway of OPnEO entering the environment.

When assessing the customer survey, it can be shown in this CSR and the points below that:

- BD analytic instruments are designed in a way that allows for the collection of liquid waste generated during operations that contain OPnEO.
- Current guidance offered by BD leads to the removal of the solid waste generated from diagnostics. This accounts for 70% of OPnEO placed on the UK market by BD.
- BD are committed to providing guidance to DUs as to how to better treat liquid waste generated by the use of BD diagnostics. It is anticipated this new guidance will remove the remaining 30% of OPnEO, resulting from liquid waste, placed on the UK market. Due to conditions currently in place for the treatment of solid waste at DU facilities it is not expected that there will be significant increased costs incurred with adhering to the new guidance.

BD are committed to the above measures and would like to clarify that the overall use of OPnEO within BD diagnostics across the UK is very small (< [redacted] [10-100] kg) per year). The above measures will provide DUs with the capability to remove OPnEO discharge that can be attributed to the use of diagnostic to all environment compartments. If customers follow the new guidance, the discharge will come as close to zero as possible. However, due to the large number of DUs BD supplies, BD would not be confident committing to a zero-discharge policy. BD feel it is not possible to micromanage such a vast number of customers. However, continued positive and proactive dialogue with DUs could get discharge rates of OPnEO that are attributed to BD to a very low number.

CBI 1

10 RISK CHARACTERISATION RELATED TO COMBINED EXPOSURE

10.1 HUMAN HEALTH

10.1.1 Workers

Not applicable – see Section 9.1.4

10.1.2 Consumer

Not applicable – see Section 9.1.5

10.2 ENVIRONMENT (COMBINED FOR ALL EMISSION SOURCES)

10.2.1 All uses (regional scale)

10.2.1.1 Total releases

The total releases to the environment from all the exposure scenarios covered are presented in the table below. This is the sum of the releases to the environment from all exposure scenarios addressed.

Table 10-1 Total releases to the environment per year from all LCS

Release route	Total releases per year
Water	[redacted][3 - 30] kg OPnEO/year [redacted][1 - 10] kg OP / year
Air	0 kg/year
Soil	0 kg/year

CBI 1

10.2.2 Regional assessment

The regional assessment is outlined in the above table.

10.2.3 Local exposure due to all widespread uses

Not relevant – due to the nature of the use of diagnostics it has not been possible to determine local exposure.

10.2.4 Local exposure due to combined uses at a site

Not relevant as there are no combined uses at either the storage facility or by the downstream users of the diagnostics.

ANNEX I - JUSTIFICATIONS FOR CONFIDENTIALITY CLAIMS

Blanked out item reference	Justification for confidentiality
CBI 1	**Demonstration of Commercial Interest:** Volumes or amount of OPnEO 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
CBI 2	**Demonstration of Commercial Interest:** Information on business commercial performance, such as manufacturing output units sold, sales, revenue and profit margins, are commercially sensitive information and are only supposed to be known by the company. If they become publicly available, they will distort competition and may even be in breach of anti-trust laws in the UK and the EU. **Demonstration of Potential Harm:** If marketing (production, sales, revenue and profits) information were to be released, it will provide the applicant's competitors with proprietary knowledge of information on the applicant's market share and would give them an unfair competitive advantage. **Limitation to Validity of Confidentiality:** This claim is valid indefinitely