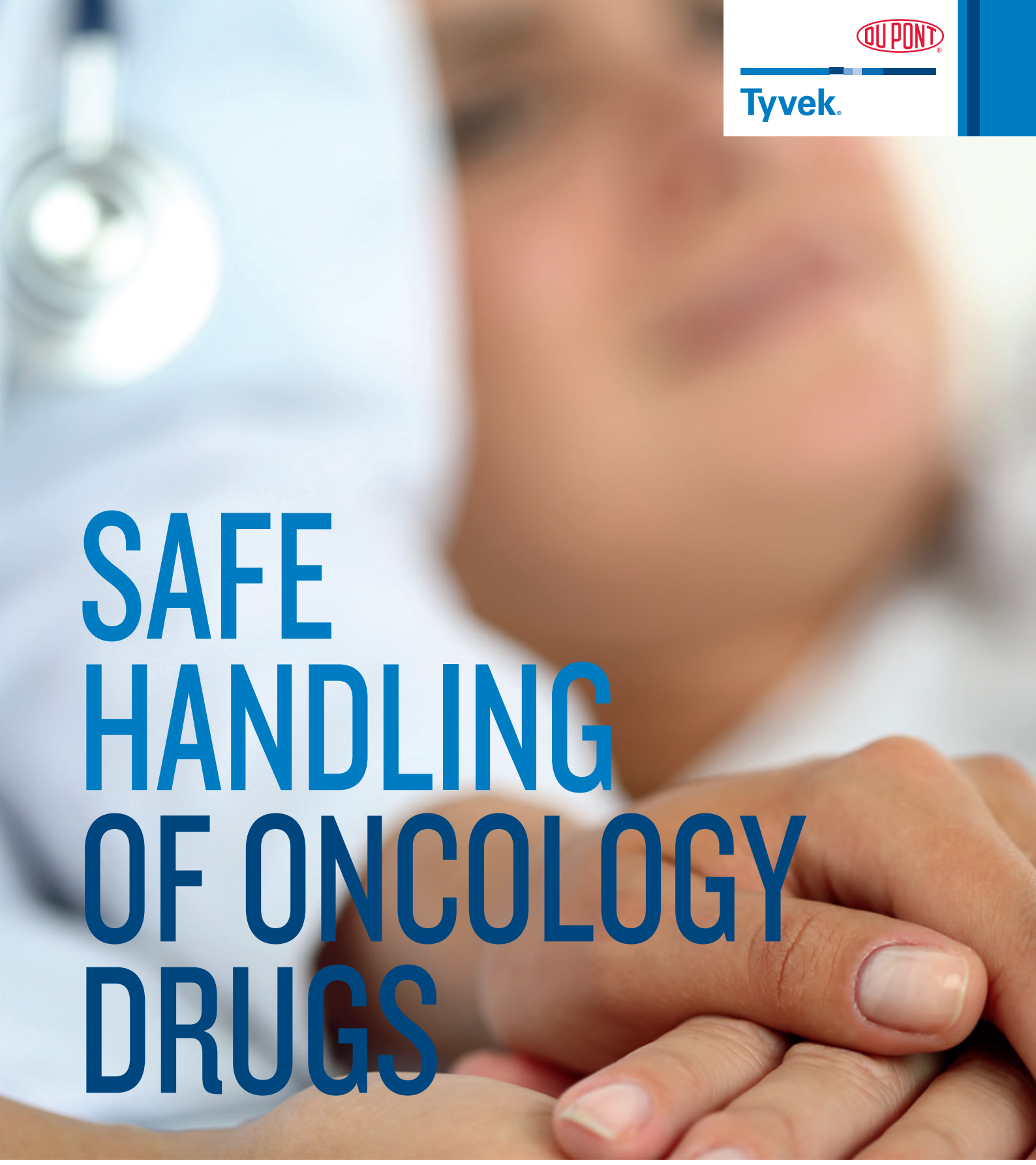


DUPONT
Tyvek®

SAFE HANDLING OF ONCOLOGY DRUGS

FOR GREATER GOOD™

Every year brings new hope and improves the outlook for patients with cancer. Advancements in biology, patient care and new treatments are key drivers to fight the battle with the world greatest healthcare challenge. Cytostatic drugs thanks to their healing power of destroying cancer cells, are considered one of the most effective ways of oncology therapies. The same substances which are lifesaving for patients, may also harm healthy cells of those involved in their handling. Three protective clothing ranges - Tyvek® IsoClean®, Tyvek® and Tychem® not only provide confidence for people involved in cancer treatments, but also protect cytostatics from contamination, to ensure the highest quality of drugs administered to patients.

Understanding the danger of cytostatic drugs handling

Without proper protection, cytostatic compounds represent a significant health risk as they can lead to abnormal formation of cells in healthy organisms, therefore are carcinogenic, mutagenic and reprotoxic. The greatest hazards arise by contact with cytostatic dusts, liquids or through aerosol formation. This brochure is intended to provide guidance on protection to all people and organizations involved in activities which can lead to contact with cytostatic substances, such as:

Pharmaceutical drug manufacturing | Drug preparation in hospitals and oncological centres | Handling ready-to-administer chemotherapy drugs to patients | Handling patient waste and waste disposal | Handling cytostatic spills and accidents | Drug transportation and storage

Minimising the risk through personal protective clothing

In the spirit of prevention being the best type of protection, every person handling cytostatic substances, no matter if pharmaceutical operator or nurse under law must be provided with appropriate technical and organisational measures and suitable CE certified personal protective equipment (PPE). The *Quality Standard for the Oncology Pharmacy Service* provides guidance on the requirements of PPE when handling cytostatic substances:

Fabric
- Low or no particle shedding
- Particle retention
- Liquid repellent (especially around arms, chest and abdomen)

Design
- Long sleeves
- Closed down the front
- Tight cuffs
- Burst proof seams

Comfort
- Breathable and comfortable to wear
- Good fit

"The directives, regulations and guidelines currently in use stipulate the use of protective equipment by every employee of a cytostatic department deriving from evaluation of the hazard involved. The PPE must carry the CE mark[1] and must be specified in writing in the hazard evaluation."
Quality Standard for the Oncology Pharmacy Service, European Society of Oncological Pharmacy, Hamburg 2014.

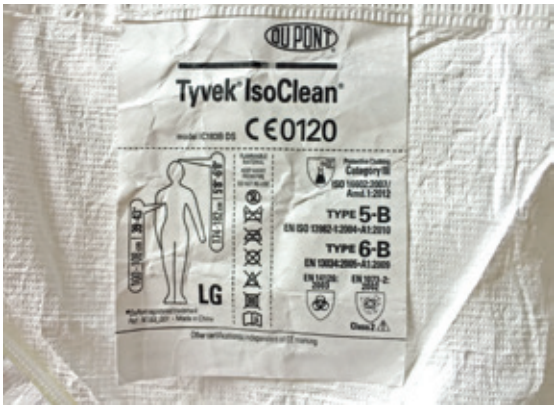
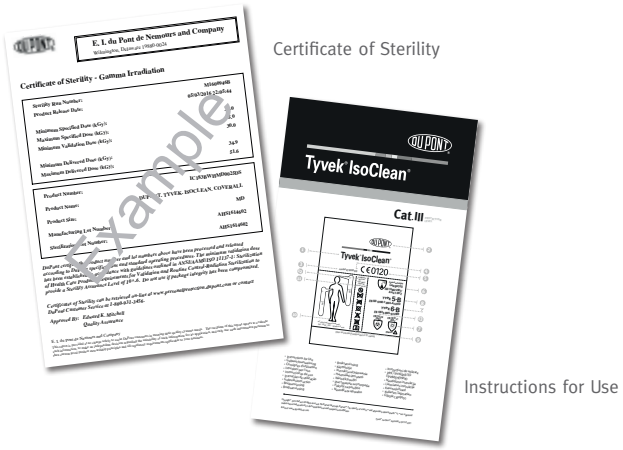


Figure 1. Example of product CE marking and documentation



Certificate of Sterility

Instructions for Use

Choosing the right protective clothing to protect people and products

Hazard evaluation and understanding all requirements associated with a specific application are essential to determine the most effective personal protective solution. Apart from protecting people, the products must also be protected from contamination by people, e.g. by skin particles, hair, lint or other particles originating from clothing. Product integrity and the relevant aseptic procedures and GMP guidelines bear the same weight as personal protective equipment. The 9 Steps presented on the next page should be followed in alignment with legislation/recommendations to arrive at the most appropriate PPE.

[1] *The PPE Directive 89/686/EEC or EU Regulation 425/2017 covers the manufacture and marketing of personal protective equipment. It defines legal obligations to ensure that PPE on the European market provides the highest level of protection against hazards. The CE marking affixed to PPE provides evidence of this protection.*

Step 1	Step 2	Step 3	Step 4	Step 5	Step 6	Step 7	Step 8	Step 9
Identify the hazard	Determine minimum levels of protection needed	Assess hazard toxicity	Determine performance requirements of the fabric	Determine mechanical performance requirements	Comfort considerations	Choose the right supplier	Identify the correct usage of the product	Perform a wear test

Figure 2. 9 steps of garment selection

Understanding protective clothing fabrics

When considering protective clothing for use with cytostatics it is crucial to know different fabric technologies as they often exhibit widely varying performance attributes. Below we present short descriptions of single use Tyvek® fabric and reusable textiles and key aspects to consider when handling cytostatics.

Reusable textiles i.e. polyester garments have a woven structure with pores. They are often subjected to multiple cycles of wearing, laundering and sterilization that can impact negatively barrier properties and durability during the garment life cycle. With reusable solutions it is also important to consider proper monitoring of garments, cleaning procedures to avoid the risk of cross contamination. Reusable polyester cleanroom clothing is typically not certified as personal protective equipment according to Directive 89/686/EEC. When personal protection is required by the task, it is recommended to wear complimentary coveralls or accessories certified as personal protective equipment.

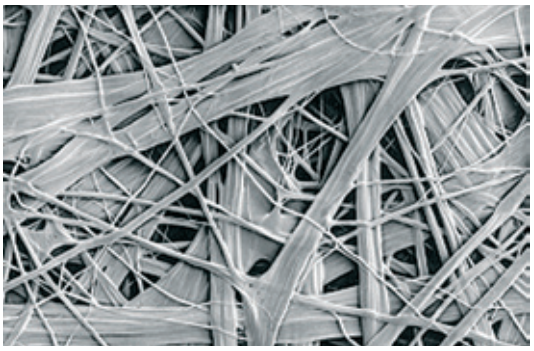


Figure 3. Tyvek® tough nonwoven material structure (high density polyethylene) 1:500 Source: DuPont.

Tyvek® due to its unique versatile material structure provides an abrasion resistant barrier. It provides a high level of protection against airborne particles >1µm and against permeation of a range of low concentrated inorganic water-based chemicals. Tyvek® garments are low-linting and have a smooth surface which provides very little foothold for particle adhesion. Tyvek® material is soft, and supple making garments much more comfortable to wear than other products. Additionally, with a bacterial filtration efficiency of > 98%, Tyvek® IsoClean® coveralls offer the ability to filter out bacteria. Moreover, CE certified Tyvek® coveralls are available as Cat. III PPE.

Permeation to cytostatic agents

PPE must be provided with appropriate technical documentation proving clothing performance properties e.g. permeation data to cytostatics. Garment specifier or user must have a clear understanding of the technical properties of the various materials that might be considered for a given application. Permeation is the process by which a chemical, in the form of a liquid, vapour or gas, moves through protective clothing material on a molecular level. Permeation is measured on fabrics used in PPE to assist with the selection of a protective fabric, garment or accessory suitable for an application as a part of the risk assessment.

In order to provide appropriate protection against a specific chemical, the chemical permeation data needs to be consulted as knowing the toxicity or consequences of short- or long-term exposure to a hazard is essential. A permeation rate indicates the mass of the chemical in micrograms (µg), which can be transferred through one square centimetre (cm^2) of the fabric in one minute (min). The unit is µg/cm^2/min. To be able to compare permeation data, the breakthrough time (BT) is reported at different normalized permeation rates - BT 0.01µg/cm^2/min, BT 0.1µg/cm^2/min and BT 1.0µg/cm^2/min.

In the table we provide data from measurements which have been conducted on critical cytostatic agents on different DuPont fabrics. The selection of cytostatic drugs and the test procedure has been based on the Standard Practice for Assessment of Resistance of Medical Gloves to Permeation by Chemotherapy drugs (ASTM D6978). Testing has been performed by independent accredited laboratories at a test temperature of 27°C according to ASTM D6978 requiring to report BT at 0.01 µg/cm^2/min or EN ISO 6529[2] requiring to report BT at 0.1 and 1.0 µg/cm^2/min. Reporting a normalized breakthrough time $BT_{0.01}$ according to ASTM D6978 is 100 times more stringent than reporting a normalized breakthrough time $BT_{1.0}$ according to EN ISO 6529.

Permeation data by hazard			Tyvek® 500 Tyvek® 600			Tyvek® 800			Tychem® C			
Hazard name	Concentration	CAS number	BT 0.01	BT 0.1	BT 1.0	BT 0.01	BT 0.1	BT 1.0	BT 0.01	BT 0.1	BT 1.0	
Carmustine	3.3 mg/ml, 10 % Ethanol	154-93-8	<10	<10	>240	>240	>240	>240	>240	>240	>240	ASTM 6978, Table 1
Cyclophosphamide	20 mg/ml	50-18-0	>240	>240	>240	>240	>240	>240	>240	>240	>240	
Doxorubicin HCl	2 mg/ml	25136-40-9	>240	>240	>240	>240	>240	>240	>240	>240	>240	
Etoposide (Toposar®, Teva)	20 mg/ml, 33.2 % (v/v) Ethanol	33419-42-0	>240	>240	>240	>240	>240	>240	>240	>240	>240	
Paclitaxel (Hospira)	6 mg/ml, 49.7 % (v/v) Ethanol	33069-62-4	>240	>240	>240	>240	>240	>240	>240	>240	>240	
Thiotepa	10 mg/ml	52-24-4	<10	<10	<10	213	>240	>240	16*	>240	>240	
Fluorouracil, 5-	50 mg/ml	51-21-8	<10	<10	47*	>240	>240	>240	>240	>240	>240	
Carboplatin	10mg/ml	441575-94-4	>240	>240	>240	>240	>240	>240	>240	>240	>240	ASTM 6978, Table 2
Cisplatin	1 mg/ml	15663-27-1	>240	>240	>240	>240	>240	>240	>240	>240	>240	
Gemicitabine	38 mg/ml	95058-81-4	<10	<60	>240	>240	>240	>240	>240	>240	>240	
Ifosfamide	50 mg/ml	3778-73-2	>240	>240	>240	>240	>240	>240	>240	>240	>240	
Irinotecan	20 mg/ml	100286-90-6	5*	>240	>240	nm	nm	nm	nm	nm	nm	
Mitomycin	0.5 mg/ml	50-07-7	>240	>240	>240	>240	>240	>240	>240	>240	>240	
Methotrexate	25 mg/ml, 0.1N NaOH	59-05-2	>240	>240	>240	>240	>240	>240	>240	>240	>240	
Vincristine sulphate	1 mg/ml	2068-78-2	>240	>240	>240	nm	nm	nm	nm	nm	nm	
Ganciclovir	3 mg/ml	82410-32-0	>240	>240	>240	nm	nm	nm	nm	nm	nm	
Oxalplatin	5 mg/ml	63121-00-6	<10	<10	<10	<10	>240	>240	145	>240	>240	
Vinorelbine	0.1 mg/ml	71486-22-1	>240	>240	>240	nm	nm	nm	nm	nm	nm	

Permeation data by hazard			Tyvek® IsoClean® 0B (non sterile, bulk)			Tyvek® IsoClean® CS Clean-processed&sterile			
Hazard name	Concentration	CAS number	BT 0.01	BT 0.1	BT 1.0	BT 0.01	BT 0.1	BT 1.0	
Carmustine	3.3 mg/ml, 10 % Ethanol	154-93-8	<10	<10	>240	<10	<10	>240	ASTM 6978, Table 1
Cyclophosphamide	20 mg/ml	50-18-0	>240	>240	>240	>240	>240	>240	
Doxorubicin HCl	2 mg/ml	25136-40-9	>240	>240	>240	>240	>240	>240	
Etoposide (Toposar®, Teva)	20 mg/ml, 33.2 % (v/v) Ethanol	33419-42-0	>240	>240	>240	>240	>240	>240	
Paclitaxel (Hospira)	6 mg/ml, 49.7 % (v/v) Ethanol	33069-62-4	>240	>240	>240	>240	>240	>240	
Thiotepa	10 mg/ml	52-24-4	<10	<10	<10	<10	<10	<10	
Fluorouracil, 5-	50 mg/ml	51-21-8	<10	<10	>240	<10	<10	<10	
Carboplatin	10mg/ml	441575-94-4	>240	>240	>240	>240	>240	>240	ASTM 6978, Table 2
Cisplatin	1 mg/ml	15663-27-1	>240	>240	>240	>240	>240	>240	
Gemicitabine	38 mg/ml	95058-81-4	<10	<60	>240	<10	<60	>240	
Ifosfamide	50 mg/ml	3778-73-2	>240	>240	>240	>240	>240	>240	
Oxalplatin	5 mg/ml	63121-00-6	<10	<10	<10	<10	<10	<10	

CAS - Chemical abstracts service registry number, > Larger than, < Smaller than, imm - Immediate (< 4 min), nm - Not tested, * Based on lowest single value
BT 0.01 - Normalized breakthrough time at 0.01 µg/cm²/min,
BT 0.1 - Normalized breakthrough time at 0.1 µg/cm²/min,
BT 1.0 Normalized breakthrough time at a permeation rate of 1.0 µg/cm²/min in minutes according to EN 14325: Protective clothing against chemicals – test methods and performance classification of chemical protective clothing: > 10 = EN Class 1; > 30 = EN Class 2; > 60 = EN Class 3; > 120 = EN Class 4; > 240 = EN Class 5; > 480 = EN Class 6.

[2]*Protective clothing - Protection against chemicals - Determination of resistance of protective clothing materials to permeation by liquids and gases*

DuPont protective clothing - solution for every need

As single-use protective clothing, Tyvek® IsoClean®, Tyvek® and Tychem® ranges of products have the advantage that uncontaminated virgin material with a proven and documented barrier protection provided for each use. Tyvek® IsoClean® coveralls are designed especially for use in cleanrooms and controlled environments demanding high levels of microbiological protection. Protective suits made of Tyvek® are also suitable for activities involved in the production of cytostatics and offer different levels of protection depending on hazard type. Accessories made of Tychem® C provide additional protection from inorganic chemicals for body parts subjected to high levels of exposure. In the next paragraphs we provide and overview of solutions, suitable for different types of applications.

Cat. III Tyvek® IsoClean® for controlled environments

Tyvek® IsoClean® coveralls offer the highest level of cleanliness within DuPont portfolio and are suitable for environments requiring a high level of microbiological protection. They are CE certified and suitable for cleanrooms up to GMP A&B, ISO 4/5, CLASS 10/100 and available in clean-processed&sterile option. Other products from the range such as, hoods, sleeves or boot covers enable full body protection from head to toe.

Tyvek® IsoClean® Coverall, model IC 183 B

- Unhooded coverall available in white, in sizes S to XXXL.
- Bound neck, internal bound seams, Tyvek® covered elasticated thumb loops, tunnelled elastication at wrists and ankles, front zipper closure with storm flap.
- Sterility Assurance Level (SAL) of 10^{6} (ISO 11137)
- Dual barrier validated packaging system for contamination control and sterility risk management (double bagged)
- Packed in an ISO Class 4 Certified Cleanroom.
- Available in Clean-Processed&Sterile option (DS) suitable for GMP A&B, ISO 4/5, CLASS 10/100 controlled environments

Chemical Protective Clothing Category III

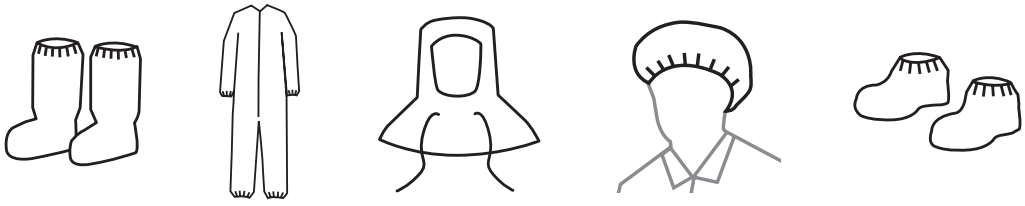
- Type 5-B
- Type 6-B
- EN 1073-2 Class 2
- EN 14126
- ISO 16602
- ISO 11137

To see the full product range please visit www.safespec.dupont.co.uk or order a free sample on www.tyvek.co.uk/isoclean

Interested in a sample or wear trial? Visit tyvek.co.uk/isoclean

A detailed examination of technical performance data and product standards is only the first part of the product selection process. A wear trial allows to evaluate the product performance in use. This will include using the garments part of an appropriate PPE ensemble to ensure full 'in-use' compatibility under expected operating conditions. The result will be a choice of garment that fulfils user expectations in terms of fit, function, comfort, performance, durability and, of course, safety.

TRY IT!



www.tyvek.co.uk/isoclean

Cat. III Tyvek® coveralls for other cytostatic applications

Tyvek® garments such as the models mentioned below, are low-linting and have a smooth surface which provides very little foothold for particle adhesion. Depending on the need, some models offer protection against liquid chemicals or liquid chemicals under pressure (Type 3 and Type 4). In addition, protective garments produced from Tyvek® can be easily sterilized using conventional methods.

Tyvek® Classic Plus, model CHA5a

- Hooded coverall available in white, in sizes S to XXXL
- Also available with integrated socks
- Stitched and over-taped seams provide the same barrier action against liquids as the suit, adhesive zipper flap with integrated chin flap
- Antistatic treatment on both sides
- Suitable for GMP C&D ISO 7/8, CLASS 10,000/ 100,000 controlled environments

Chemical Protective Clothing Category III

- Type 4-B
- Type 5-B
- Type 6-B
- EN 1149-5
- EN 1073-2 Class 2
- EN 14126

Tyvek® 800 J, model CHA5

- Hooded coverall available in white, in sizes S to XXXL
- Self-adhesive zipper flap, self-adhesive chin flap for tight seal of suit to mask, elasticated
- Antistatic treatment on the inside
- Suitable for GMP C&D ISO 7/8, CLASS 10,000/ 100,000 controlled environments

Chemical Protective Clothing Category III

- Type 3-B
- Type 4-B
- Type 5-B
- Type 6-B
- EN 1149-5
- EN 1073-2 Class 2
- EN 14126

Tyvek® Labo, model CHF7

- Hooded coverall available in white, in sizes S to XXXL
- Internal seams to reduce contamination, integrated slip-retardant shoe covers, tunnelled
- Antistatic treatment on both sides
- Suitable for GMP C&D ISO 7/8, CLASS 10,000/ 100,000 controlled environments

Chemical Protective Clothing Category III

- Type 5
- Type 6
- EN 1149-5
- EN 1073-2 Class 2

To see the full product range please visit www.safespec.dupont.co.uk

Cat. III Tychem® complimentary protection for applications with high exposure levels

Tychem® C consists of a Tyvek® substrate with a polymer barrier coating and is 100% particle-tight. It provides protection against a wide range of inorganic chemicals and biological hazards. Accessories made of Tychem® C, such as sleeves or back-fastening gowns provide additional protection for parts of the body subjected to particularly high levels of exposure.

Tychem® C gown, model PL50

- Available in yellow and sizes S/M and L/XXL
- Shin-length gown with wrap-over rear closure, hook and loop neck closure and waist ties, elasticated wrists

Cat. III Type PB[3] Partial body protection

Tychem® C sleeve, model PS32LA

- Available in yellow and in one size
- 50 cm long and with wide elastics at cuffs and upper arm

Cat. III Type PB[3] Partial body protection

For protection against organic and highly concentrated inorganic chemicals and biological hazards Tychem® F range is also available. To see the full product range please visit www.safespec.dupont.co.uk

Cat. I Tyvek® IsoClean® accessories

Tyvek® IsoClean® Frock, model IC 270 B

- Frock available in white in sizes S to XXXL
- Bound neck, bound seams, covered elastication at wrists, front snap closure for easy donning and doffing
- Available in 2 options: Clean-Processed&Sterile (MS) suitable for GMP A&B, ISO 4/5, CLASS 10/100 controlled environments and Non-sterile -bulk (0B) suitable for GMP C&D ISO 7/8, CLASS 10,000/ 100,000 controlled environments

Cat. I PPE

Tyvek® IsoClean® Sleeve, model IC 501 B

- Sleeve available in white and in one size
- Bound seams, tunnelled elastication at wrist and bicep
- Available in 2 options: Clean-Processed&Sterile (MS) suitable for GMP A&B, ISO 4/5, CLASS 10/100 controlled environments and Non-sterile - bulk (0B) suitable for GMP C&D ISO 7/8, CLASS 10,000/ 100,000 controlled environments

Cat. I PPE

Tyvek® IsoClean® Hood, model IC 668 B

- Hood available in white and in one size
- Bound seams, bound hood opening, full face opening, ties with loops for adjustable fit
- Available in 2 options: Clean-Processed&Sterile (MS) suitable for GMP A&B, ISO 4/5, CLASS 10/100 controlled environments and Non-sterile -bulk (0B) suitable for GMP C&D ISO 7/8, CLASS 10,000/ 100,000 controlled environments

Cat. I PPE

To see the full product range please visit www.safespec.dupont.co.uk or order a free sample on www.tyvek.co.uk/isoclean

Need help in risk assessment and garment selection?

DuPont offers a range of support tools to assist with risk assessment and garment selection: ranging from web-based tools and on-site risk assessment support with DuPont Personal Protection specialists and chemists, to chemical permeation barrier testing for your specific chemicals.

Try DuPont™ SafeSPEC™

SafeSPEC™ is an online product catalogue and interactive tool that will help you with the risk assessment. Browse and compare products by brand, design or certification, with direct access to all relevant product information and literature, including cytostatic permeation data.

DuPont™ SafeSPEC™

www.safespec.dupont.co.uk

Important Note
The permeation data published have been generated for DuPont by independent accredited testing laboratories according to the test method applicable at that time (EN369, ASTM F739, EN 374-3, EN ISO 6529 (method A and B) or ASTM D6978). The data is typically the average of three fabric samples tested. Cytostatic drugs testing have been performed at a test temperature of 27°C according to ASTM 6978 or according to EN ISO 6529 with the additional reporting of a normalized breakthrough time at 0.01 µg/cm²/min. A different temperature may have significant influence on the breakthrough time. Permeation typically increases with temperature. Permeation data are usually measured for single chemicals. The permeation characteristics of mixtures can often deviate considerably from the behaviour of the individual chemicals.
Permeation data for Tyvek® is applicable to white Tyvek® only and is not applicable for other Tyvek® styles or colours. Breakthrough time is not the same as safe wear time. Breakthrough time alone is insufficient to determine how long a garment may be worn once the garment has been contaminated. Safe user wear time may be longer or shorter than the breakthrough time depending on the permeation behaviour of the substance, the toxicity of the substance and the exposure conditions. Breakthrough times are indicative of the barrier performance, but results can vary between the test methods and laboratories.
Please use the permeation data as part of the risk assessment to assist the selection of a protective fabric, garment or accessory suitable for your application. Working conditions, exposure conditions (e.g. temperature, pressure, concentration, physical state), and the toxicity data for the chemical need to be taken into account.
The information provided herein corresponds to our knowledge on the subject at the date of its publication. This information may be subject to revision as new knowledge and experience becomes available. The data provided fall within the normal range of product properties and relate only to the specific material designated; these data may not be valid for such material used in combination with any other materials or additives or in any process, unless expressly indicated otherwise. The data provided should not be used to establish specification limits or used alone as the basis of design; they are not intended to substitute for any testing you may need to conduct to determine for yourself the suitability of a specific material for your particular purposes. Since DuPont cannot anticipate all variations in actual end-use conditions DuPont makes no warranties and assumes no liability in connection with any use of this information. Nothing in this publication is to be considered as a license to operate under or a recommendation to infringe any patent rights.

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