DuPont Personal Protection

The HSE Manager's Guide to Protective Garments for Pharmaceutical Applications

How to Protect Workers Against Hazardous Substances and Prevent Contamination

New technologies, novel diseases, and innovative medical treatments are transforming the pharmaceutical industry.

Now more than ever, pharmaceutical companies must protect their workers against multiple chemical and biological hazards while maintaining the highest levels of cleanliness. Personal Protective Equipment (PPE) is critical to protecting workers while preventing contamination. This e-guide looks at the key factors Health, Safety and Environment (HSE) managers in the pharmaceutical industry should consider when selecting protective garments for their workers.

The first section examines exposure and contamination risks in pharmaceutical applications and the relevant legislation and guidelines. The guide then focuses on two pharmaceutical sectors: vaccine manufacturing and oncology drug production. Both sectors are experiencing significant growth and undergoing important changes with health and safety implications. The guide analyzes each application, the main risks to workers, the potential for contamination, and how the latest garment solutions can help address them.

Content overview

1/ Hazardous Substances and Contamination Risk in Pharmaceutical Applications

In the pharmaceutical industry, HSE management has three fundamental objectives:

1. keeping workers safe from hazardous substances;
2. preventing the accidental contamination of pharmaceutical products and processes;
3. constantly checking and re-evaluating work procedures to take into consideration changes to production processes, reclassifications of hazardous substances and new regulations.

A hazardous substance can either be chemical or biological and is defined by the EU-OSHA as "any liquid, gas or solid that poses a risk to workers' health or safety"[1]. The CLP Regulation[2] groups dangerous substances into three main categories:

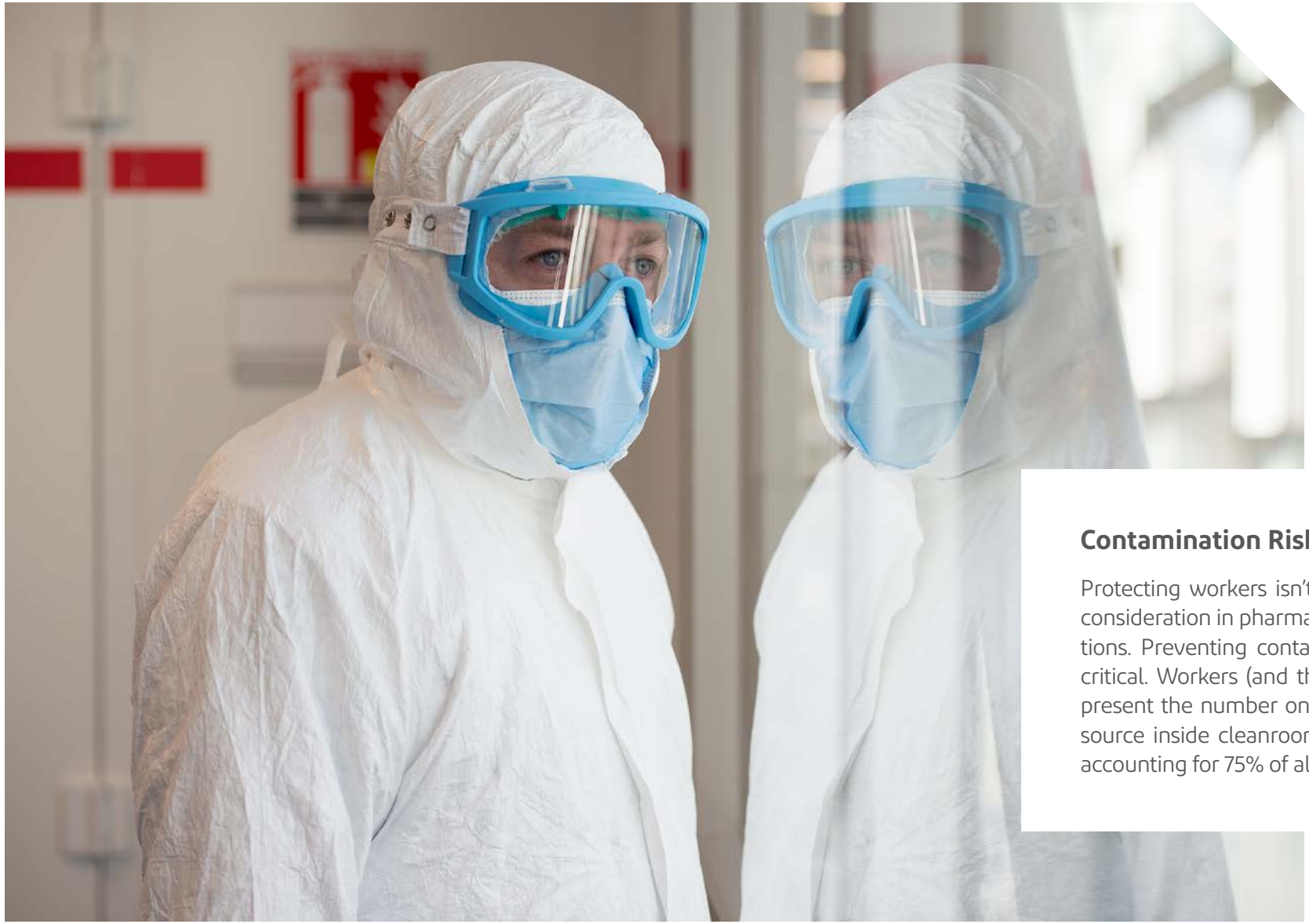
- physical hazards (explosive, flammable, unstable, etc.);
- health hazards (all aspects of short- and long-term harm to health);
- environmental hazards (aquatic environment, etc.).

This guide focuses primarily on "health hazards" prevalent in pharmaceutical applications.

Exposure to a dangerous chemical or biological agent can cause severe illness[3], including:

- Allergies;
- Skin diseases;
- Cancers;
- Reproductive problems.

High potency active pharmaceutical ingredients (HPAPI) are among the most dangerous substances. These agents can lead to serious health effects even at low concentrations[4]. As the global demand for HPAPI continues to grow[5], protecting workers in pharmaceutical manufacturing has never been so important.



Contamination Risk

Protecting workers isn't the only safety consideration in pharmaceutical applications. Preventing contamination is also critical. Workers (and their clothing) represent the number one contamination source inside cleanroom environments, accounting for 75% of all contaminants[6].

2/ Health and Safety Legislation and Guidance

In Europe, dangerous chemicals are regulated under the REACH legislation (Registration, Evaluation, Authorisation, and Restriction of Chemicals)[7]. This norm mandates that companies identify and manage the risks associated with the substances they manufacture, use or import.

The EU has also adopted specific legislation to protect workers from carcinogens, mutagens, and reprotoxic (CMR) substances, including hazardous pharmaceutical products. Directive 2004/37/EC[8] mandates that employers must take necessary measures to protect workers against CMR, such as:

- performing a risk assessment;
- putting in place preventive measures;
- providing health and safety training and appropriate protective clothing.

New Legislation

In March 2022, the EU Council approved an amendment to Directive 2004/37/EC[9]. The new legislation introduces exposure limits for widely-used acrylonitrile and nickel compounds. It also lowers existing limits for benzene and provides greater protection against reprotoxic substances. In addition, the directive mandates that workers dealing with hazardous medicinal products must receive better training on how to handle them safely.

3/ Protective Clothing: an Essential Component of Personal Protection

PPE is critical to protecting workers in pharmaceutical environments. According to the COSHH (Control of Substances Hazardous to Health) legislation, equipment like protective clothing is the last line of defense against dangerous substances and "should be used when all other measures are inadequate to control exposure"[10].

Additionally, PPE such as protective clothing should prevent contamination of the surrounding environment. Contamination can occur when particles are shed by the human body or the PPE itself.

The final version of the EU's Good Manufacturing Practice (GMP) Annex 1 guideline, covering the current regulatory and technological developments in the manufacture of sterile medicine products[11] was published on 25 August 2022. Pharmaceutical manufacturers will be expected to proactively identify and control potential risks to quality associated with cleanroom garment systems, in line with QRM (Quality Risk Management) principles.

Let's now examine two specific examples of pharmaceutical applications, the specific risks involved, and the protective garment solutions.

3.1. Vaccine Manufacturing

The production of vaccines has experienced unprecedented growth during the COVID-19 pandemic. This important sector is likely to continue to expand, driven by the WHO's target to achieve 70% COVID-19 immunisation coverage by mid-2022[12].

Messenger RNA (mRNA) vaccines have proven a game-changer in the fight against COVID-19. Unlike conventional vaccines, the RNA type is produced using chemical processes that don't require a cell culture system or high-level biosafety containment, making the process faster and easier[13]. However, this new technology requires hazardous active ingredients and organic reagents (like enzymes). Selecting appropriate protective clothing is critical to safeguarding workers against these substances. Here are some important considerations:

- Ensure that the garment is CE-certified as category III (protective clothing intended to protect against serious or fatal risks).
- Depending on the application and risk level, opt for garments that offer protection against aqueous liquids and liquid aerosols (see Table 1 for more information).
- Choose materials like high-density polyethylene filaments providing strong barrier properties. For instance, DuPont™ Tyvek® filaments are thermally bonded into a tight, homogeneous fabric that protects the wearer against any particles larger than 1 micron.

Table 1: Know Your Labels

Pictogram*	Type	Definition and Exposure Level	Product Standard and Year of Publication
	TYPE 1 TYPE 1 - ET	**GAS-TIGHT** TYPE 1 – Protective clothing against liquid and gaseous chemicals, including liquid aerosols and solid particles. TYPE 1 - ET – Performance requirements for emergency teams.	EN 943-1:2019** EN 943-2:2019
	TYPE 2	**NON-GAS-TIGHT** Protective clothing against liquid and gaseous chemicals, including liquid aerosols and solid particles.	EN 943-1:2019**
	TYPE 3	**LIQUID TIGHT** Protective clothing against liquid chemicals. Exposure to pressurised jet of liquid.	EN 14605:2005/A1:2009
	TYPE 4	**SPRAY TIGHT** Protective clothing against liquid chemicals. Exposure to a liquid spray aerosol (unpressurised).	EN 14605:2005/A1:2009
	TYPE 5	**SOLID PARTICULATES** Protective clothing against solid-airborne particulates.	EN ISO 13982-1:2004/A1:2010
	TYPE 6	Limited protective performance against liquid chemicals Potential exposure to small quantities of fine spray/mist or accidental low volume splashes and where wearers are able to take timely adequate action in case of contamination.	EN 13034:2005/A1:2009

In vaccine manufacturing, preventing contamination in sterile cleanroom environments is essential. To minimise the risk of particle shedding, select the cleanroom garment systems that are GMP compliant including garments meeting following criteria:

- suitable for different cleanroom types (GMP A/B, C/D);
- thoroughly tested to provide a barrier against contamination generated by the operators, both in terms of particle filtration efficiency (PFE) and bacterial filtration efficiency (BFE);
- thoroughly tested to ensure a low risk of particle shedding;
- abrasion and tear-resistant, minimising the risk of particle shedding.

The most common way of evaluating the performance of cleanroom garments is the Helmke drum test, which measures the particles generated by the garment itself. The particle filtration efficiency (PFE) test (EN143) and the bacterial filtration efficiency (BFE) test (ASTM F2101) assess the garment's ability to prevent particle shedding generated by the wearer. A more reliable testing method is the Body Box (IEST-RP-CC003.4), which simultaneously assesses particle shedding from the garment and the wearer and the garment's PFE and BFE. The latest DuPont™ Tyvek® IsoClean® garments display exceptional Body Box test results, even during knee bends.

Comfort is another important consideration. Wearing uncomfortable garments can lead to fatigue, a common cause of injuries and sweating, which increases particle shedding. Cleanroom garments made using Tyvek® are lightweight, soft, and breathable, ensuring optimal comfort for operators.

3.2 Oncology Drug Production and Preparation

Demand for oncology drugs is growing, and cancer treatments are constantly evolving, with 64 new active substances launching globally over the past five years[14]. Drugs are becoming more effective but are also posing new challenges to HSE managers throughout the pharmaceutical supply chain, from manufacturing to hospital pharmacies.

For example, cytostatic compounds are now widely used in oncology drugs. These substances are carcinogenic, mutagenic, and reprotoxic, posing a threat to workers. Exposure to cytostatic dust, liquids, or aerosol formation presents the greatest risk.

Antibody-drug conjugates (ADCs) are another recently-developed cancer treatment[15] that pose risks to workers, due to the use of powdered cytotoxic reagents[16]. According to the Health and Safety Executive[17], healthcare workers in hospital pharmacies are particularly at risk. Exposure typically occurs through skin contact, skin absorption, inhalation of aerosols and drug particles, or needle stick injuries during:

- drug preparation and administration;
- handling and disposing of patient waste;
- cleaning spills.

Exposure to cytotoxic substances can have direct consequences, ranging from contact dermatitis and allergic reactions to miscarriage or foetal malformations in pregnant women[18].

As for vaccine manufacturing applications, category III clothing is essential to protect workers dealing with oncology drugs while preventing contamination. Specific requirements may vary depending on the worker's task and the risks involved. Typically, workers in oncology drugs manufacturing applications may require:

- solutions combining a high level of protection (Type 4-B, 5-B and 6-B) with the enhanced comfort of a nonwoven suit;
- garments equipped with chemical-resistant socks ensuring that the feet are fully sealed and protected against dangerous substances while helping prevent contamination;
- stitched and overtaped seams providing the same barrier performance as fabric or bound seams, reducing the risk of particle shedding;
- a hood shape and elastic that provides a tight fit around the respirator, ensuring optimal protection and preventing contamination;
- Tunnelled elastics, cuff, ankles, and face, reducing the risk of contamination.

For workers in laboratory and cleanroom environments, additional features to consider may include:

- an innovative "feel-good effect" design for greater comfort and flexibility;
- extremely high-quality control specifications;
- attached overshoes with slip-retardant soles.

Comfort may not be the top priority for workers undertaking maintenance or cleaning tasks (e.g. maintenance of pipes or reactors) as they typically wear protective clothing for short periods of time. However, these workers will require a higher level of protection than other workers as they face a greater risk of exposure to dangerous compounds. Clothing should:

- come with a rubber seal offering good compatibility with a full face mask;
- be equipped with sealed-in gloves for full-body protection;
- not require taping, enabling faster donning in emergencies;
- feature rear entry with double flaps for enhanced protection against frontal exposure;
- attached dissipative socks with boot flap.

4/ Conclusion

The pharmaceutical industry is constantly evolving to meet today's challenges. Innovation enables the development of new drugs to treat diseases more effectively, from COVID-19 to cancer. But the widespread use of high potency active pharmaceutical ingredients poses added threats to workers, from pharmaceutical manufacturing to hospital pharmacies. PPE such as protective clothing has a critical role in protecting workers while preventing contamination, which may compromise the quality and safety of medicinal products. Global suppliers like DuPont Personal Protection have the expertise and technology to enable pharmaceutical companies to take health and safety to the next level.

For more information on DuPont™ Tyvek® solutions for the pharmaceutical industry visit: dpp.dupont.com.

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