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GETINGE ISOCYT FREJA
THE SAFEST WAY TO PROTECT BOTH PATIENT AND PHARMACIST

Always with you

PROTECT THE PATIENT.
PROTECT THE PHARMACIST.
PROTECT THE PLANET.

Cytotoxic drugs are an occupational health hazard. And since there is growing evidence that traditional drug preparation systems are not safe enough for health workers when handling cytotoxics, more and more hospital pharmacies realize what Getinge La Calhène has known since the 80's: that the safety of both the patient and the pharmacist can only be fully assured by separating the compounding from the operator with a true physical barrier.

The growing use of cytotoxic preparations adds a new component to the preparation and administration process: protection for the workers who work with the drugs. Cytotoxic drugs are very harmful to healthy humans; some are mutagenic, carcinogenic and-or teratogenic (may cause birth defects).

This creates a hazardous working environment for the staff who routinely handle them. Studies have shown that even when using protective clothing and a biosafety cabinet BSC II, personnel become contaminated with the chemicals.

The solution: advanced isolation technology

Over the years since Getinge La Calhène developed the first hospital pharmacy isolator in 1985, the pharmaceutical industry have adopted and expanded the application requirements for isolation technology.

Getinge La Calhène have been at the forefront of this development, and our knowledge and experience in the field of isolation technology for GMP production has grown significantly, together with that of our clients.

Today, our ISOCYT systems for drug compounding and reconstitution in hospital pharmacies are widely used all over the world. Now, we present the latest addition to the ISOCYT series – the Getinge ISOCYT FREJA. A compact and productive system that provides the same sterility assurance level as in pharmaceutical manufacturing. A really safe and cost-efficient solution, that also offers better ergonomics, easier installation and lower operating costs.


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WHY IS ISOLATION TECHNOLOGY A BETTER ALTERNATIVE THAN OTHER SYSTEMS?

The risks associated with handlng of cytotoxics has been studied in detail and documented. The issue is how to manage that risk in the most efficient manner. Management of risks and management of costs – it's a delicate balance. Operational efficiency, safety, workflow, ergonomics and cost are examples of factors that must be considered.

Traditional preparation systems

For more than 20 years, Class II Biological Safety Cabinets (BSC) have been used for the local preparation of drugs in hospital pharmacies. By default, these have continued to be used for the preparation of cytotoxics. However, evidence continues to grow that such systems are inherently unsafe for this application: spillage, aerosol release during vial and syringe venting, as well as waste disposal all contribute to the release of hazardous chemicals into the working environment. This is a well documented and scientifically proven fact.

Moreover, maintenance of a clean environment (clean room) for the preparation area is costly:

- Floor space (incl. changing areas) and ventilation to maintain ISO class 6 (required class for BSC II)
- Consumables – gowns, masks, cleaning agents
- Loss of productivity due to gowning in-out
- Restrictions in access to clean area

Isolation Technology

An isolator provides a physical separation of a process from the environment – in this application providing a barrier around the compounding process, keeping contamination (e.g. microbial) away from the product, protecting product quality, whilst simultaneously protecting the operator and environment from the dangerous chemicals. By their very nature a BSC (having an aperture) cannot achieve this level of separation. Benefits of isolators include (c/w BSC installation):

- The ability to maintain a sterile environment, without compromising the sterility assurance level of the components (drug, diluent and administration kit). = lower risk of nosocomial infection in patients who are generally already immunodepressed
- Repeatable, validatable production according to GMP
- A class 8 cleanroom installation with considerably less restrictions / monitoring / running costs than class 6
- Less floor space required for preparation area
- Reduced consumables (gowns, masks, etc)
- Possibility to re-use opened vials (short term storage) = Significant cost saving potential
- Improved waste management – completely safe disposal of empty containers, spill mats, bags, etc
- Whilst isolators have a higher capital cost, running costs are significantly lower; the payback on capital investment can be achieved in as little as 1 year. Consult Getinge for a study of your production and life cycle cost analysis.


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ISOCYT FREJA – A NEW CONCEPT IN CYTOTOXIC RECONSTITUTION

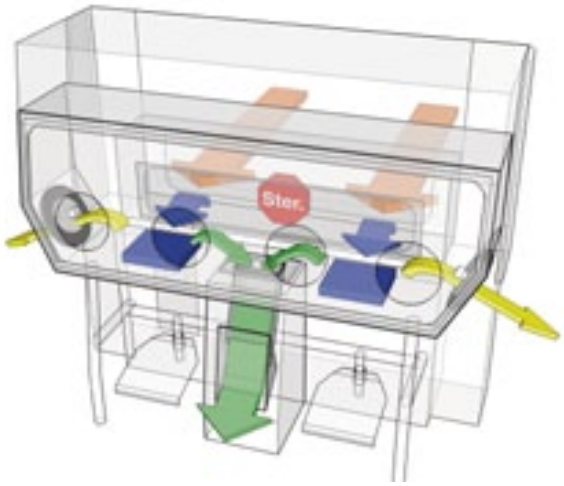
Isolation technology is a complex issue and there are always many, many solutions to a challenge: some better than others. Both vendors and clients have opinions based on their experiences in making or using isolators. Getinge have combined these views and experiences, and have developed ISOCYT FREJA, a dedicated isolator for preparation of personalised cytotoxic medication, with the following objectives:

- To satisfy the therapeutic needs of the growing number of cancer patients using a wider and growing range of treatments
- To protect healthcare workers from the harmful effects of these treatments on healthy humans
- To assure the quality and safety of these treatments by maintaining a high Sterility Assurance Level for the drug, solvent and administration system
- To satisfy the ever-increasing regulatory demands required for the preparation / administration of these treatments (e.g. requirement to follow Good Manufacturing Practice, GMP)

ISOCYT FREJA is suitable for local hospital pharmacies (e.g. outpatient/ambulatory), cancer clinics, regional production centres and independent service providers. It is designed for high productivity and maximum safety while complying with all current GMP requirements.

Design Principles of ISOCYT FREJA:

- **Optimum throughput**
  50 reconstitutions or more may be performed per day (depending on protocols, organization of hospital, etc.).
- **Dual workstations**
  Two operators sit side-by-side, each with their own access to materials from the bio-decontamination transfer port (drug, diluent, administration kit, utensils), secure waste disposal port, and output port.
- **Bio-decontamination airlock**
  For bio-decontamination of external surfaces of drug and diluent containers (contents are sterile), administration kit and utensils using the integral Getinge Steritrace II system.
- **Robust construction**
  Rugged stainless steel and glass construction.
- **Control system for flow and pressure control**
  Siemens PLC control system for reliability, repeatability and accuracy. Positive or negative pressure control with turbulent flow.
- **Transfer ports**
- Dynamic port for output of completed prescriptions (optional DPTE® bagging output, with heat sealer).
- DPTE® "Dispobag" for secure removal of waste.



FAQ – Design Criteria Questions Answered

• CONSTRUCTION
We selected stainless steel and glass over plastic for (a) ruggedness in the work environment and (b) for the shortest possible bio-decontamination time (HPV is absorbed into plastic material, taking longer to desorb)

• UNIDIRECTIONAL OR TURBULENT FLOW
We selected turbulent flow as unidirectional (laminar) flow is unnecessary for this application (and adds to complexity). Circulated air is HEPA filtered, assuring that the environment is particle free.

• POSITIVE OR NEGATIVE PRESSURE
The isolator may be controlled under positive (product protection) or negative (environment protection) pressure.
Getinge's philosophy (default settng) is to control at positive pressure.
Leak testing of the isolator is a standard function.
In the unlikely event of a leak due to system defect or incorrect operation, the isolator enters an emergency mode with negative pressure control and maximum exhaust ventilation.

WHY “FREJA”

Freja is the mythological Nordic Goddess of Love, Beauty and Fertility. She is regarded as a force for good in the world – protector of the weak, healer, and source of love and peace. This is fitting for the ISOCYT isolator, which protects both sick patients and healthcare workers, the latter also from pregnancy problems and birth defects, which can result from contact with teratogenic drugs.

DESIGNED FOR THE BEST OPERATIONAL EFFICIENCY

1. Robust stainless steel and glass construction
Robust stainless steel frame and isolator body. Isolator chamber is polished internally and has radiused corners for easy cleaning. The front panel is tempered glass, which is internally illuminated through a further glass panel in the top of the chamber (external light for easy replacement).

Two workstations are provided, each accessing the chamber via comfortable sleeves and gloves. Each station has access to the central output port and an individual waste disposal port.

2. Dynamic Output Port
Completed prescriptions are rapidly passed out of the isolator through a central dynamic transfer port. Product is placed in the port from inside the isolator, and then removed from the port via a door on the front.

A controlled pressure cascade ensures that the integrity of the isolator is not compromised during the passage of the reconstitution.

As an option, a DPTE® bagging port (**6**), complete with heat sealer, may be provided for one or both workstations (individual options). The output port is located above the waste outlet.

This allows product to be removed rapidly and aseptically in a heat – sealed, pre-sterilized bag.

3. DPTE® Waste Port And Trolley

Waste is removed from the isolator using two industry standard DPTE® ports – one at each workstation – for safe removal and transportation to an incinerator.

DPTE® ports provide leaktight, aseptic transfer that are mechanically interlocked to prevent improper operation. See page 12 for a detailed description.

A DPTE® Dispobag® is connected to each port to receive the (toxic) waste. Each bag is supported in a purpose designed transparent trolley (for visual indication).

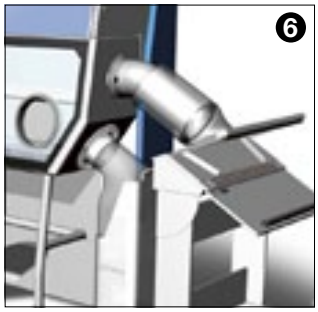
When full, the bag may be removed for incineration without disturbing isolator (or bag) integrity and allowing operation to continue without interruption.

4. Gloves

Gloves are replaceable without breaking containment. These may be replaced in-process, saving time, maximizing productivity.

5. Adjustable footrests

Each workstation is equipped with independentlly adjustable footrests providing a comfortable, ergonomic working position for the operator. Each footrest is fitted with a non slip mat.



INNOVATIVE BIODECONTAMINATION AIRLOCK AND NEW INTEGRATED STERILIZATION SYSTEM

7. Getinge Steritrace II HPV Sterilization System
ISOCYT FREJA is equipped with an automatic cost effective, integrated system for bio-decontamination of both isolator and transfer airlock.

The system uses hydrogen peroxide (H_2O_2) vapor (HPV) as sterilant. HPV is generated from liquid H_2O_2 from a bottle which is placed in a receptacle on the isolator.

Developed by Getinge La Calhène, the integral generator is controlled by the same PLC as the isolator, minimizing components and requiring validation and maintenance of only a single piece of equipment.

HPV is a proven sterilant, commonly used in pharmaceutical industry applications. It is compatible with most common materials, colorless, odorless and simple to monitor during equipment qualification.

Prior to use, a bottle of liquid Hydrogen Peroxide is placed in a receptacle in the isolator (**7**).

The bottle is fitted with an RFID device containing a batch number and expiration date of the liquid (H_2O_2 degrades over time).

The generator checks if the date is valid and the batch number is recorded in the process report.

The Steritrace II provides a reproducible and validatable process for both routine biodecontamination of the transfer airlock and periodic biodecontamination of the isolator chamber.

Note: An external sensor is available for environmental/operator safety. Available from Getinge as an option

8. Siemens PLC Controller And Touchscreen Display

Both the isolator and integral Getinge Steritrace II HPV sterilizer are controlled by a single Siemens PLC control system. This assures repeatable, reliable operation. The Siemens PLC is an industry standard and has communication capabilities for remote monitoring.

The operator control panel is a 7" touchscreen, which provides access to the PLC for parameter setting (by authorized persons) and critical parameter monitoring. Alarms are also clearly presented on the display.

The single, easily navigated operator panel assure simple operation, minimized errors, and maximized productivity.

9. Bio-decontamination Transfer Airlock

A single bio-decontamination transfer airlock, opened from rear to allow input of materials, is provided opposite and within easy reach of both operators.

The airlock extends across the width of the isolator but is shallow enough to allow easy access to all parts. The design also facilitates easy cleaning.

During preparation for a campaign, the door of the airlock is opened from outside the isolator and materials for the procedure are placed inside.

A biodecontamination cycle is performed using the integral Steritrace II system (**6**). Typical process time is 20 minutes. Shorter cycles for emergency cases can be developed according to your requirements.

On completion, the materials are transferred to the isolator chamber from inside. A simple system of red-green lights indicates when the door may be opened.

As soon as the materials are removed, a new batch may be processed while the operators are working with the first batch, maximising productivity (no waiting time).

Biodecontamination, Sterilization and Sterile

In a healthcare context, decontamination is a means of rendering material safe to handle. Contaminants may be hazardous chemicals or biological agents. Bio-decontamination is a means of removing biological agents.

- Sterilization is one of several bio-decontamination processes.
- "Sterile" is defined as a complete absence of living organisms. As microbial destruction is a logarithmic function, it is not absolute, but the accepted level to define a product 'sterile' is a log-6 reduction (a spore log reduction, or SRL, of 10^6)

Injectable products must be "Sterile". To render an injectable drug "sterile", it must be either terminally sterilized (e.g autoclaved after packaging), or must be produced in an aseptic environment.

In "aseptic processing" the drug is sterilized (e.g. by filtration), and the packaging is pre-sterilized. The environment for the packaging must be controlled to prevent opportunity for contamination.

An isolator optimally separates the preparation environment from the external surroundings. An isolator may be readily bio-decontaminated to reduce the bio-burden, and may be maintained in this condition (through appropriate transfer technologies) for extended periods. It is more practical to achieve this in an isolator compared to a clean room, hence, the achievable SAL is higher for aseptic processing in an isolator compared to a clean room. Product sterility may be assured.

Typically, bio-decontamination of the environment is performed at an SAL of 10^6 (sterile), but 10^4 is sometimes allowed for operational efficiency purposes.

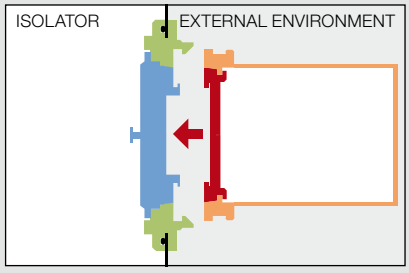
Getinge's Steritrace II is capable of providing a sterilization process for an isolated environment and we refer to it as an "integrated H_2O_2 sterilizer".

Getinge will as standard provide a bio-decontamination process at an SAL of 10^6. However, clients may, based on a risk assessment, decide to decontaminate at a lower level (e.g. 10^4)

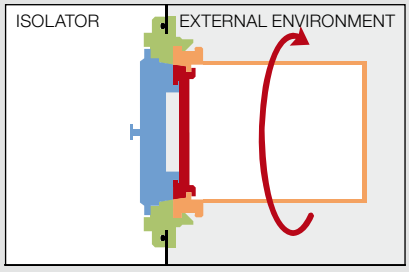
HPV bio-decontamination is superior to other bio-decontamination techniques (such as alcohol wipedown) as it is repeatable, validatable and not dependent on manual procedure.

DTPE® TRANSFER TECHNOLOGY – A CRUCIAL SUCCESS FACTOR

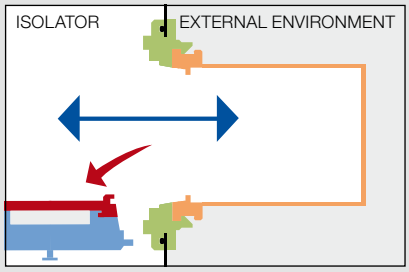
While providing significant safety and contamination control benefits, placing a physical barrier between the process and the user introduces operational challenges: how to move material into and out of an isolator without breaking the sterile containment? And how to provide easy, comfortable manipulation while maintaining good operational efficiency?



Picture 1 shows the containerapproach to the isolator and its Alpha port.



Picture 2 shows the interlocking of the two ports by a 60-degree rotation.



Picture 3 shows the interlocked doors being opened, allowing safe/sterile exchange of materials.

ALPHA BETA

Fortunately this is nothing new for Getinge La Calhène. Many years ago, La Calhène developed a system that has become an industry standard worldwide. Originally built for transporting radioactive material for the nuclear industry (where Getinge La Calhène remains a key supplier), the DPTE® System is now also used for a wide variety of life science applications where toxic or aseptic material is being transferred. Widely known as an Alpha-Beta or RTP port, it is now used for a wide variety of applications in the pharmaceutical industry where toxic and-or sterile material needs to be transferred. The “Beta” port (see diagram) may be attached to a container for product input or output, or to a bag for secure waste removal.

GETINGE
– YOUR UNIQUELY QUALIFIED SUPPLIER

Getinge is a world leader in Contamination Control. At one end of this broad spectrum, we supply healthcare institutions with cleaning and disinfection equipment for hospital wards and theatres, while at the other, we supply the global pharmaceutical industry with systems and solutions for drug manufacture according to GMP requirements.

This combination uniquely positions Getinge as a qualified supplier to hospital pharmacies, where patient care meets drug preparation.

In this regulated environment, pharmacists must prepare drugs according to the same principles of quality control and safety as pharmaceutical companies, while at the same time delivering personalised care to sick patients.

Getinge's expertise; our qualifications

As a world leader in the field of cleaning and sterilization, Getinge draws from over 100 years of accumulated knowledge to provide the advanced equipment, application skills, documentation, regulatory know-how and support services you can depend on.

Getinge La Calhène

During the late 1970's the French company La Calhène developed the first pharmaceutical isolator systems based on long experience from the nuclear industry. Since then, isolator technology from La Calhène has been used in many applications in healthcare and research institutions and pharmaceutical factories all over the world. The company has rightfully earned its worldwide reputation for being instrumental in the development of isolation technology to prevent cross-contamination between manufactured products and their environment. La Calhène joined the Getinge family in 2005, creating Getinge La Calhène. The combination provides Getinge's clients with new possibilities to provide protection to healthcare workers and the environment while providing high quality care and safety for patients.

ACCESSORIES, CONSUMABLES, CONTINUOUS SUPPORT AND SERVICE

Installation, commissioning and qualification services are provided by our global network of sales and service support companies and representatives.

Training is provided by the Getinge Academy, an organisation with regional centers, run and staffed by professional trainers.

Our core business idea could be summarized in one sentence: To keep our clients safe and operationally effective. We spare no effort to obtain this. Everything we do must be related to this aspect of our customer relationship. Integrated solutions, continuous assessments and upgrades, well-defined quality systems and efficient service programs are some pillars of this philosophy. Rapid system integration, a high degree of technical compatibility and swift consumable and spare part delivery are others.

Our Philosophy

Getinge's aim is not only to provide high quality, industry leading, reliable equipment, our objective is to be your chosen partner within specific application areas of Infection and Contamination control.

Our products and services are available globally, provided and supported by 27 Getinge sales and service companies and a network of more than 65 authorized distributors. We presently distribute and support our products locally in more than 100 countries.

Our Scope of Supply

In addition to the ISOCYT FREJA isolator,
we can also provide:

- Installation, commissioning and qualification services
- Routine maintenance and periodic validation
- Training, carried out by our professional Academy
- A wide range of accessories, including baskets, racks, glove and port testing equipment
- Spare parts, delivered rapidly from our regional distribution centers
- Consumables, incl. zip pouches, dispobags, gloves & sleeves, cleaning kits, steriliant, filters, baskets

RELATED PRODUCTS FROM GETINGE FOR PHARMACY PRODUCTION UNITS

Big Brother: The Getinge ISOCYT3 is no need for hyphen in "reconstitutions" designed for higher capacity productoion – typically up to 100 reconstitutions per day.

Getinge offer a wide range of cleaning and sterilization equipment, both for laboratory and GMP production applications, including Terminal Sterilization.

The modern pharmacy production unit, whether based in a local hospital, regional center, or as an independent service provider has a need to manufacture safe and effective drug products. Moreover, there is an ever increasing focus on safety, ergonomics and productivity: produce the most, with the least resources at the minimum cost, but with a quality assured product.

Mission Impossible? Now more, than ever, our clients need a reliable, focused supplier who has the process knowledge as well as the product range to take responsibility for the application.

Getinge: a unique supplier

As was highlighted earlier in this brochure, Getinge is uniquely positioned as a supplier to Hospital Pharmacies and related production centers.

We are a world leader in the manufacture and supply of equipment for Healthcare applications, in particular in relation to equipment for Infection and Contamination Control.

Furthermore, we are a leading supplier to the Pharmaceutical Industry, with an intimate knowledge of Good Manufacturing Practice, in particular for liquid injectable (parenteral) products.

And as mentioned on the adjacent page, we are global!

The complete production chain

Getinge can take care of virtually all your needs in the sterile processing of pharmaceuticals. We supply:

- Water pretreatment & distillation systems
- Pharmaceutical steam generators
- Component and equipment washers & sterilizers
- Laboratory washers & sterilizers
- Terminal sterilization equipment

In addition to the ISOCYT FREJA isolator, we also manufacture and supply isolators for larger scale production facilities, for example, the ISOCYT3. Consult Getinge for details.

COMPLETE SOLUTIONS FOR CONTAMINATION PREVENTION

Getinge is the world's leading provider of solutions for effective cleaning, disinfection and sterilization in the healthcare and life science sectors. We are dedicated to helping our customers provide maximum productivity in the most cost-efficient way. We do this by offering well thought through and customized solutions. This means that we are with our customers all the way from architectural planning and education to traceability and support – with complete solutions, long-term commitment and global presence. Getinge – Always with you.

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GETINGE GROUP is a leading global provider of products and systems that contribute to quality enhancement and cost efficiency within healthcare and life sciences. We operate under the three brands of ArjoHuntleigh, GETINGE and MAQUET. **ArjoHuntleigh** focuses on patient mobility and wound management solutions. **GETINGE** provides solutions for infection control within healthcare and contamination prevention within life sciences. **MAQUET** specializes in solutions, therapies and products for surgical interventions, interventional cardiology and intensive care.

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