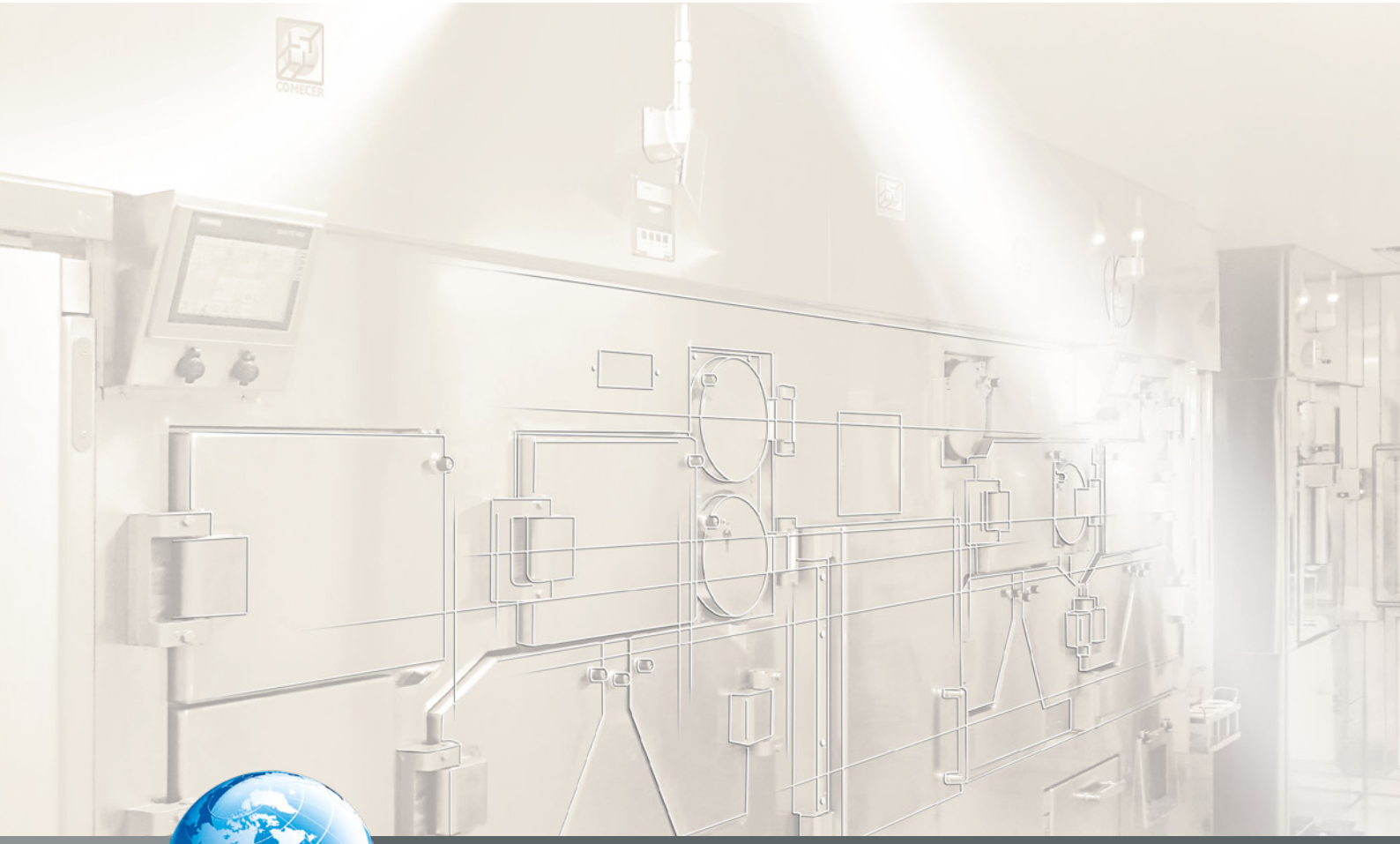
INDUSTRIAL PROJECTS FOR

RADIOPHARMACEUTICAL PRODUCTION PLANTS



END TO END **CUSTOM PROJECTS**

COMECER

AN ATS COMPANY

^{99}Mo DISPENSING, PACKAGING AND STORAGE PLANT

AUSTRALIA

Production plant consisting of two high-shielding hot cells in which it is possible to perform fractionation, calibration and preparation operations for shipment of ^{99}Mo bulk.

The system can safely handle up to 65 TBq of ^{99}Mo and is equipped with special dose calibrators to measure these extreme activities. Due to the high gamma emission in the chamber, the hot cell is made with appropriate design considerations on materials and components capable of withstanding high doses of ionizing radiation. It is also built and validated with appropriate safety systems (SIL-3 ref IEC 61508) for monitoring and related interlocking on access points and airlocks. It is possible to safely connect 1.2 Tons transport flask through a door on the ceiling. The cell is also equipped with waste extraction systems and a connection door for B(U) containers that can be adapted to different formats.

Number of working chambers: 3 + 2
Type of process:
- Non sterile API manufacturing

Type of shielding:
- Lead 180 mm / Lead 150 mm

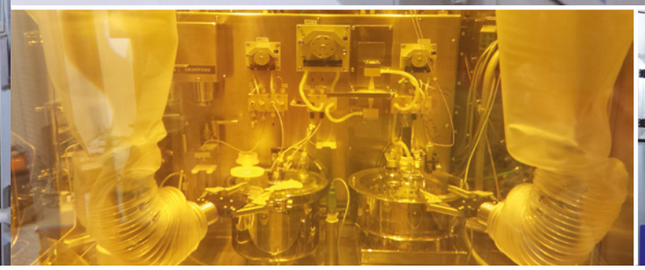
Automation systems available:
- containment handling of B(U) transport containers

Particularly interesting features:
- handling up to 65 TBq ^{99}Mo
- “SIL-3”-certified safety interlocks according to IEC 61508

Productivity:
- Up to 20 multi-dose / batch vials.

^{99m}TC GENERATOR PRODUCTION PLANT

POLAND



Semi-automatic line for the production of ^{99m}Tc generators in GMP. The plant allows the loading from B(U) of the ^{99}Mo bulk, the formulation and adjustment of the chemical parameters of the solution, the loading of the ^{99}Mo in the generator column, the autoclave sterilization of the columns, the semi-automatic assembly and the 100% QC verification of each generator. The line is therefore equipped with a series of progressive-shielding chambers able to keep safe all the plant interlocking operations, from the high-activity bulk loading to the final washing and QC operations. The double pass-through autoclave allows a transfer of the loaded columns with a one-way transfer of the material for an optimal process flow and the possibility to guarantee the productive reliability also in case of maintenance of one of the two autoclaves.

Number of working chambers: 12
Type of process:
- Terminal sterilization

Type of shielding:
- Lead 150 mm / Lead 100 mm

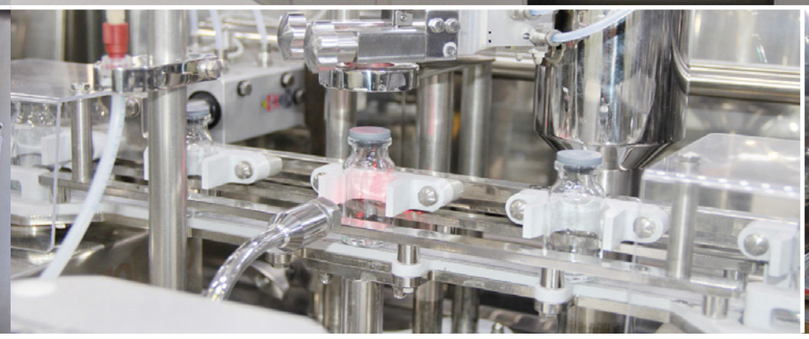
Automation systems available:
- Automatic ^{99}Mo formulation
- Automatic filling of generator columns
- Automatic washing of generator columns

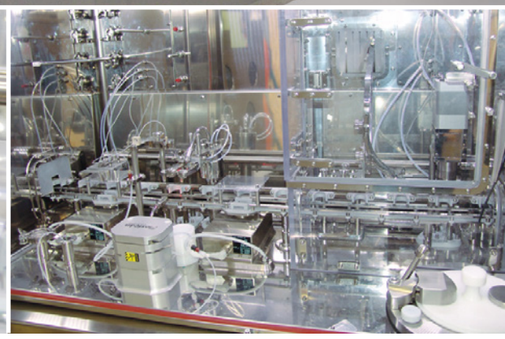
Particularly interesting features:
- Automatic in-line QC for ^{99}Mo breakthrough during filling

Productivity:
- 250 generators in 12 h, 3 batch per week.

CardioGen-82® ^{82}Rb GENERATOR PRODUCTION PLANT

USA





Plant for the production of ^{82}Sr/^{82}Rb generators consisting of several shielded isolators interconnected with each other. The column is loaded in an aseptic area (Class A - ISO 5) and the plant production process and design comply with GMP and FDA requirements. The production process includes the loading and automatic formulation in the non-sterile area, through hot cells equipped with high shielding and telemanipulators, and an aseptic area where the column loading and washing takes place. Subsequently, a series of conveyors and automatic assembly stations assist the operator during all the phases, allowing the construction of the generator and the final verification of QC and sterility of the finished product. Thanks to the integrated vaporized H_2O_2 generators, the aseptic chambers can be sterilised automatically and the material loaded in a sterile condition.

Number of working chambers: 8
Type of process:
- "Aseptic manufacturing"

Type of shielding:
- Lead 125 mm / Lead 75 mm / Lead 50 mm

Automation systems available:
- Automatic ^{82}Sr formulation
- Automatic filling of generator columns
- Automatic washing of generator columns

Particularly interesting features:
- QC in line
- Sterility Testing In-line

Productivity:
- 100 generators in 8 h, 3 batch per week.

AUTOMATED DatScan™ IOFLUPANE ^{123}I INJECTION PRODUCTION AND DISPENSING PLANT

USA

The DatScan™ radiopharmaceutical production line is a highly automated plant for dispensing batches of 500 vials at a speed of 360 vials per hour. The plant is composed of shielded isolators in which transport, aseptic filling, visual inspection and labelling systems are integrated. The radiopharmaceutical formulation part integrates devices to perform the formulation and labelling process of the ^{123}I in a fully automatic way. The system involves the use of 4 HPLC, disposable pipes, valves and peristaltic pumps. The aseptic dispensing part meets all the requirements of sterile pharma production lines and uses a continuous feed system where vial de-capping, filling with weight feedback, capping and crimping operations take place. The vial is then buffered through a Cartesian robotic system to allow a semi-automatic visual inspection over the entire batch to verify the absence of particulate matter and aesthetic defects. Finally, the vials leaving the inspection area are labelled and placed in the transport container.

Number of working chambers: 12
Type of process:
- "Aseptic manufacturing"

Type of shielding:
- Lead 75 mm / Lead 50 mm / Lead 30 mm

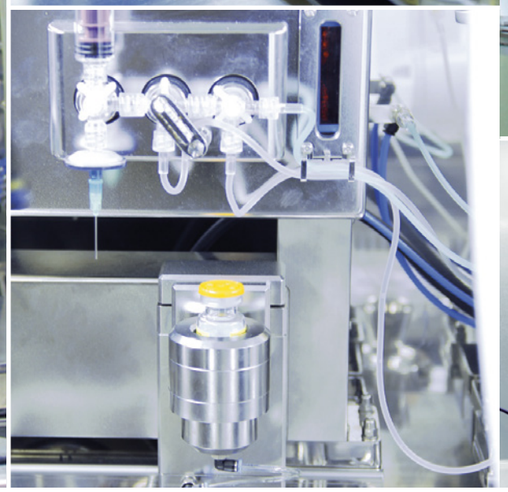
Automation systems available:
- Automatic synthesis and purification of ^{123}I Ioflupane by HPLC process
- Automatic vial filling machine, including vial stoppering, capping and crimping, 100% weight control
- Dispensing mode in open and closed vials
- Automatic buffer for 500 vials
- Semi-automatic Visual Inspection (VI)
- Automatic vial and shielded container labelling
- Automatic vial discharge in automatic container

Particularly interesting features:
- Management and development of HPLC purification in automatic
- Scale up and process chemistry development
- Automatic bulk formulation management
- Decontamination with VPHP
- Format changeover management with considerable reduction in operator radio-exposure
- Semi-automatic visual inspection of radioactive product

Productivity:
- 6 vials / minute in dispensing (filling 2,5 ml)
- 4 vials / minute in VI, labelling and packaging.

AUTOMATED ^{123}I IOFLUPANE PRODUCTION AND DISPENSING PLANT

GERMANY



Production line equipped with shielded isolators for the formulation and aseptic production in class A - ISO 5. A robotic system has been integrated in the filling area, which serves two independent medium-speed dispensers. The overall result is an ^{123}I Ioflupane dispensing system which can guarantee both high production speed (180 vials / hour) and robustness and production reliability thanks to the double independent dispenser module. The dispensing system is based on sterile disposables and is suitable for decontamination by means of vaporized H_2O_2, in accordance with GMP requirements for an aseptic dispensing. Thanks to the simultaneous multiple discharge of 4 vials with low shielding, it is possible to maintain a high productivity even with a single operator on the plant.

Number of working chambers: 3
Type of process:
- "Aseptic manufacturing"

Type of shielding:
- Lead 50 mm

Automation systems available:
- Double semi-automatic dispenser interlocked by a 6-axis anthropomorphic robot

Particularly interesting features:
- Automatic double unloading, 4 vials per rack
- Bulk common to both dispensers
- Possibility to produce in single or double dispenser mode (depending on the size of the batch)
- Automatic interlocking of trays with empty vials through the robot

Productivity:
- 3 vials / minute dispensed (filling 2,5 ml), batch 220 vials.

^{123}I IOFLUPANE PRODUCTION AND DISPENSING PLANT

USA | FRANCE

^{123}I Ioflupane production line consisting of two shielded isolators in which it is possible to carry out a formulation and dispensing process in an aseptic area. The plant is designed to meet GMP requirements and is integrated with a vaporized H_2O_2 decontamination system. The high containment ventilation system (double filtering with bag-in/bag-out) is specific for production plants that must necessarily take into account volatile isotopes such as iodine and specific installation requirements of industrial nuclear plants. The handling is managed through a set of front tele-pliers installed following an ergonomic evaluation on the process, mock-up and study of the operational dynamics. There are RTP and airlock doors that allow the discharge of the finished product and the waste management in the utmost safety.

Number of working chambers: 2
Type of process:
- "Aseptic manufacturing"

Type of shielding:
- Lead 50 mm

Automation systems available:
- vials semi-automatic dispenser

Particularly interesting features:
- Decontamination with VPHP

Productivity:
- Semi-automatic dispensing system (operator dependent).

XOFIGO® ^{223}Ra DICHLORIDE PRODUCTION AND DISPENSING PLANT

USA

The production plant covers the entire ^{223}Ra dichloride production process starting from ^{227}Ac sources stored or introduced in the initial part of the plant. The system is composed of a series of high-containment isolators, shielded and equipped with adequate alpha-emitters ventilation. In the formulation part, a separation and purification process is carried out thanks to integrated "wet" chemistry modules. The product formulated in bulk, ready for dispensing, is stored in bags connected to devices that allow a constant mixing and blending of the same. The filling phase, starting from open vials introduced in batches, consists of an automatic filling system that includes the stoppering and crimping phase and 100% check of the dispensed weight. The feeding and dispensing system is easy to clean while ensuring an easy format change (10 ml or 20 ml vials). This type of system can also be suitable for aseptic dispensing inside Class A - ISO 5 isolators. The line is integrated with a double pass-through autoclave that allows terminal sterilization in accordance with GMP guidelines. The plant speed of 1000 vials/hour inevitably requires the presence of an end-of-line system for vial labelling, insertion into the shielded transport container, verification of external contamination of the vial and final delivery to the packaging area. In the formulation phase, the product is separated and purified

Number of working chambers: 12
Type of process:
- Terminal sterilization

Type of shielding:
- Lead 80 mm - / Lead 40 mm

Automation systems available:
- Semi-automatic "wet-chemistry" modules for extraction and purification of ^{223}Ra
- Automatic management of 20 l bulk in bags, with mixing and blending before and during dispensing
- Automatic vial filling machine, including vial stoppering, capping and crimping, 100% weight control

Particularly interesting features:
- Working chambers for handling and preparation of ^{227}Ac ^{223}Ra generators
- Ventilation for alpha isotopes
- Containment for alpha isotopes
- Handling-compliant material introduction and extraction management for alpha isotopes using RTP systems

Productivity:
- vials dispensing up to 17 vials per minute (filling 6 ml).

^{90}Y AND ^{177}Lu C.A. SEMIAUTOMATIC PRODUCTION AND DISPENSING PLANT

POLAND

Production line consisting of 5 interconnected hot cells with internal doors divided into two areas and dedicated to the production of ^{90}Y and ^{177}Lu C.A. The external ones are dedicated to the formulation of individual isotopes which, through the intermediate doors, converge into a central cell in which a terminal sterilization process is possible by means of an autoclave and subsequent discharge. The formulation part includes micro-dispensers and peristaltic pump dispensing systems capable of supporting the operator in the preparation, formulation and dispensing phases. Given the particular nature and difficult management of highly concentrated radio-isotopes such as ^{90}Y and ^{177}Lu, it is necessary to manage micro-volumes and therefore employ specific devices such as automatic micro-pipettors. The presence of extremely acidic compounds in the separation process of ^{90}Sr/^{90}Y and formulation inside the isolator, makes it necessary to have an anti-acid coating on the metal parts and chambers made of plastic material (ideal also for the presence of beta emitters). In addition, appropriate ventilation and filtration are available to reduce highly corrosive fumes. Airlock and handling systems allow the correct introduction and extraction of the starting material irradiated in liquid or solid form, such as ampoules of ^{176}Lu irradiated inside reactors.

Number of working chambers: 5
Type of process:
- Terminal sterilization

Type of shielding:
- Lead 80 mm / Lead 50 mm

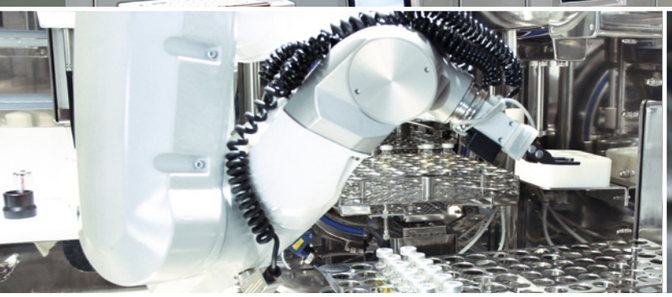
Automation systems available:
- Automatic cutting system for irradiated quartz ampoule

Particularly interesting features:
- Semi-automatic dispensing of volumes in the range of microliters for radioactive product
- Handling management of highly concentrated and corrosive substances, at room temperature and in evaporation
- Protective acid-proof coating with fluoropolymer (ventilation)
- Working chambers made of plastic material resistant to radiation, corrosion and able to provide shielding to beta-radiation

Productivity:
- 104 vials per batch, semi-automatic process (operator dependent).

^{177}Lu C.A. AUTOMATIC PRODUCTION AND DISPENSING PLANT

THE NETHERLANDS



The production plant is one of the most advanced automatic systems for large-scale production of ^{177}Lu C.A. The line is divided into two hot cells in which the process of extraction of ^{177}Lu from a ^{176}Lu ampoule irradiated in the reactor takes place and a cell for dispensing and terminal sterilization by means of autoclave. Both the formulation and dispensing cells are equipped with anthropomorphic robots that completely avoid the need for handling by operators. The ^{177}Lu extraction phase begins with the loading of the ampoule, involves a series of automated steps defined by the customer and ends with the passage of a highly-concentrated bulk in the filling chamber, also by means of automatic systems. In the dispensing chamber one or more robots in combination with automatic micro-pipettors divide the bulk in quantities of a few microliters and proceed to a dilution following the production recipe defined in the batch. The presence of one or more autoclaves, automatically loaded and unloaded, allows the end of the production process, thus guaranteeing the sterility of the product. The system then proceeds to the extraction of the vial that is unloaded into appropriate shielded containers, removed and labelled by the operator.

Number of working chambers: 2
Type of process:
- Terminal sterilization

Type of shielding:
- Lead 50 mm / Lead 30 mm

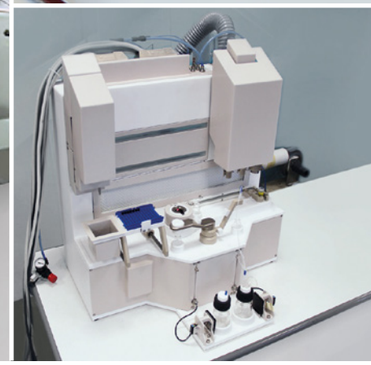
Automation systems available:
- Automatic cutting system for irradiated quartz ampoule in a dedicated containment system, separated from the working chamber
- Automatic manipulation by 6-axis anthropomorphic robot of the irradiated quartz target, calibration, dissolution, stirring, bulk transfer without any operator intervention
- Automatic dispensing, autoclave loading and unloading and unloading into shielded outlet containers using 6-axis anthropomorphic robots

Particularly interesting features:
- Protective acid-proof coating with fluoropolymer (ventilation)
- Automatic dispensing of volumes in the range of microliters for radioactive product
- Handling management of highly-concentrated and corrosive substances at room temperature
- Redundant dispensing system

Productivity:
- 160 vials in 6,5 hours, terminal sterilization included.

^{177}Lu N.C.A. SEMIAUTOMATIC PRODUCTION AND DISPENSING PLANT

SOUTH AFRICA | AUSTRALIA | GERMANY



The plant consists of 2 hot cells, one dedicated to the extraction and purification of the product, one dedicated to the dispensing and terminal sterilization. The part related to the extraction of the product is a cell equipped with a tele-pliers and dose calibrator, completely protected with an acid-proof coating based on fluoropolymers. It is designed to integrate a customer-specific module for the separation of ^{176}Yb from ^{177}Lu. The cell handles high quantities of liquid and solid wastes in appropriate separate compartments, necessary in this type of production process. The dispensing cell integrates tele-manipulators and an automated micro-pipettor module used to dispense concentrated radioisotope micro-doses and automatically proceed to the subsequent dilution, following a batch recipe set in the control system. The operator then proceeds only to the handling of the product vials and to the loading and unloading of the autoclave.

Number of working chambers: 2
Type of process:
- Terminal sterilization

Type of shielding:
- Lead 75 mm / Lead 50 mm

Automation systems available:
- Arrangement for automatic extraction and purification system supplied by the customer.
- Semi-automatic dispenser for volumes of radioactive product in the range of microliters

Particularly interesting features:
- Handling management of highly concentrated and corrosive substances, at room temperature and in evaporation
- Protective acid-proof coating with fluoropolymer (ventilation)
- Semi-automatic dispensing of volumes in the range of microliters for radioactive product
- “SIL-2”-certified safety interlocks according to IEC 61508

Productivity:
- 50 vials in 8 hours, terminal sterilization included.

COMECER
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