Medium Scale Facility for aseptic Production of Mo-99/Tc-99m Generators

Figure 1: Sample Picture of the production Line

The common type of Mo-99/Tc-99m-generator is the chromatographic one. In the described facility a dry chromatographic Mo-99/Tc-99m-generator is produced. This sterile Mo-99/Tc-99m-generator is a convenient source to obtain a sterile, pyrogen-free and isotonic [Tc-99m] NaTcO4 eluate solution, which is immediately ready for oral or intravenous administration or for aseptic production of [Tc-99m]technetium labeled radiopharmaceutical preparations. Essential part of the Mo-99/Tc-99m-generator is a sterile chromatographic column of glass with an Al2O3 sorbent on which radioactive [Mo-99]molybdenum is firmly fixed after loading with [Mo-99]Na2MoO4 loading solution. The chromate-graphic column is surrounded by lead shielding. The Mo-99/Tc-99m-generator posses an additional bacteriological filter to ensure the sterility of the [Tc-99m]NaTcO4 eluate. This eluate can be extracted in regular intervals and in a very comfortable manner by using a vial containing the required volume of sterile isotonic NaCl solution.

Eckert & Ziegler

Isotope Technologies Dresden

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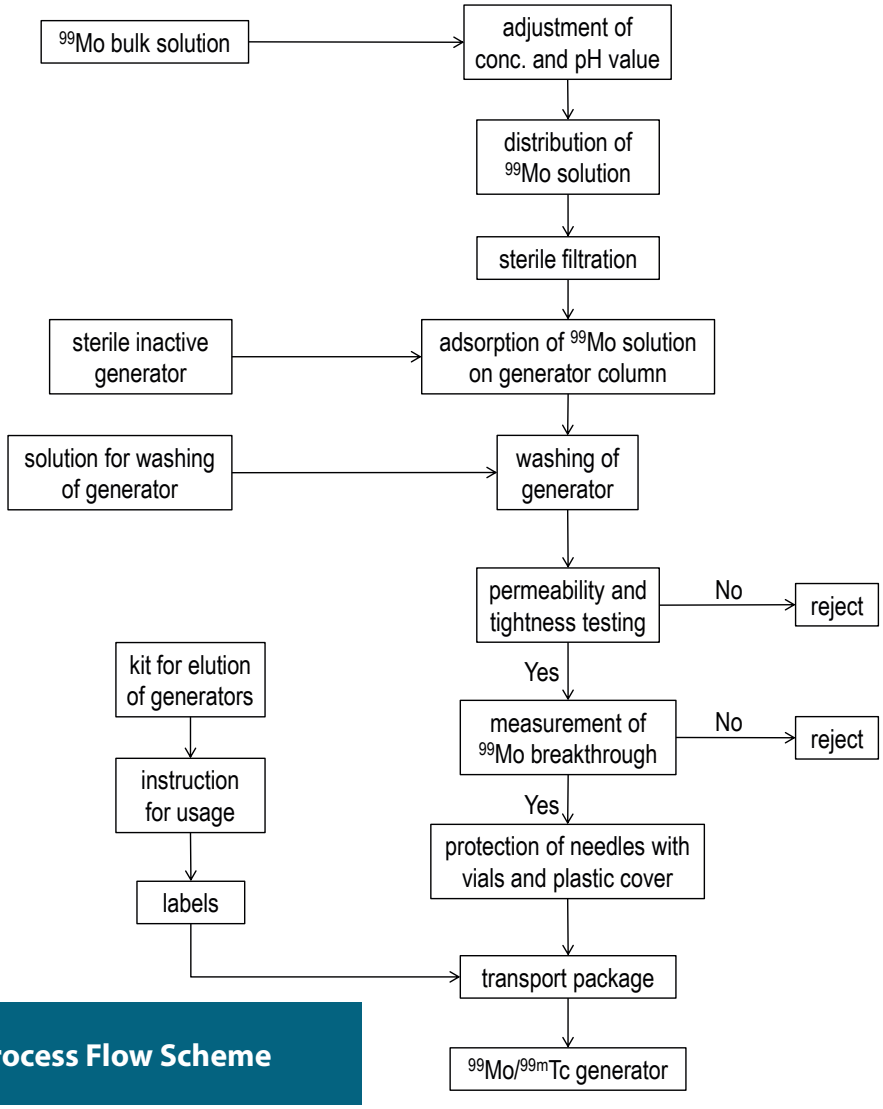

Figure 2: Process Flow Scheme

Methods

The loading of such a sterile chromatographic generator can be carried out in different ways. There is the possibility to apply either aseptic column loading procedures or procedures which include the steam sterilization of the loaded column. The process steps are quite different and require different equipment inside and outside the hot cells, especially in the clean room and sterilization equipment. For the small-medium scale production batches (20-50 pcs.) the aseptic column loading procedure was chosen, instead of a procedure with steam sterilization of the loaded column, which is rather suitable when a large scale production is established. The aseptic loading and washing process with a complete preassembled sterile generator has the advantage that the production personnel have to carry out fewer operations on the radioactive sterile generator and hence there is a significant reduction of the radiation exposure to them. In fig. 1 the main steps of the aseptic procedure are shown. It starts with the preassembly of the inactive generators. In the first hot cell the formulation of the Mo-99 solution takes place. After sterile filtration the prepared Mo-99 solution is loaded onto the generators in the second hot cell. This is followed by the washing of the loaded generators. In a locally shielded glove box a QC elution of the generators is carried out, for testing of the permeability and a Mo-99 breakthrough measurement. After the QC the needles are protected and a cover is added. Outside of the hot cell / glove box unit the produced generators are packed into type A transport packages and the user equipment and manual are added.

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The aseptic loading procedure is carried out in an advanced hot cell/glove box arrangement (fig. 2) for full compliance to the current GMP requirements. It has a special design which offers the suitable clean room barriers with adequate pressure gradients maintaining the necessary clean room environment and shielding for radiation safety. The first hot cell (dispensing box) is located in a room of clean room class "D". In this hot cell the import of the Mo-99 bulk solution and its formulation is carried out under clean room class "C". The second hot cell (loading box) and the corresponding glove boxes (PMMA box 1-4) are installed in a clean room of class "C". On a rail system the presterilized generator components entering glove box 1 with clean room class "B" and glove box 2 were the inactive generators are preassembled under clean room class "A" conditions with laminar air flow (LAF). Inside the second hot cell under clean room class "A" conditions with LAF the preassembled generators are loaded with sterile filtered Mo-99 solution and washed. The loaded and washed generators are tested for permeability and Mo-99 breakthrough in glove box 3 (clean room class "A" with LAF). Via glove box 4 (clean room class "B" with LAF) the produced generators are locked out for packaging.

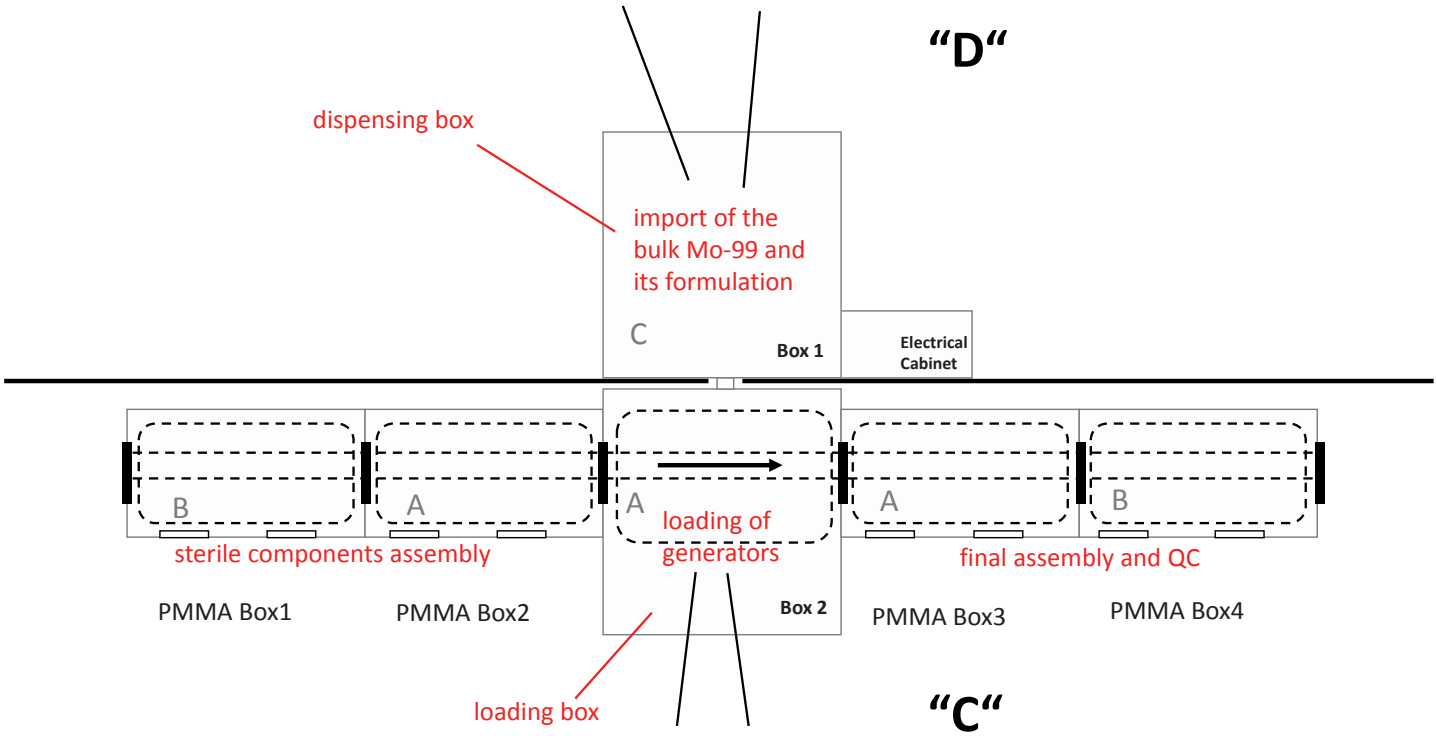

Figure 3: Hot Cell/Glove Box Arrangement Scheme

The shielding of the hot cells is made of 100 mm thick lead for the vertical walls, 70 mm thick lead for the bottom and ceiling walls. This shielding meets the international requirements to keep the radiation exposure to the operators below 5 µSv/h at any time (with max. 2500 GBq of Mo-99). The dispensing and the loading hot cell are separated by a wall with a lead shielding of 50 mm. In fig. 3 an example of the intended hot cell / glove box arrangement installed in a class "C" clean room is shown. There are access doors in order to open the hot cells for maintenance purposes. The windows of the hot cells are made of 230 mm thick lead glass with a density of 5.2 g/cm3. Below the hot cells bottom there is sufficient space for waste collecting containers. The docking unit for Mo-99 transport containers is designed for docking of different types of containers.

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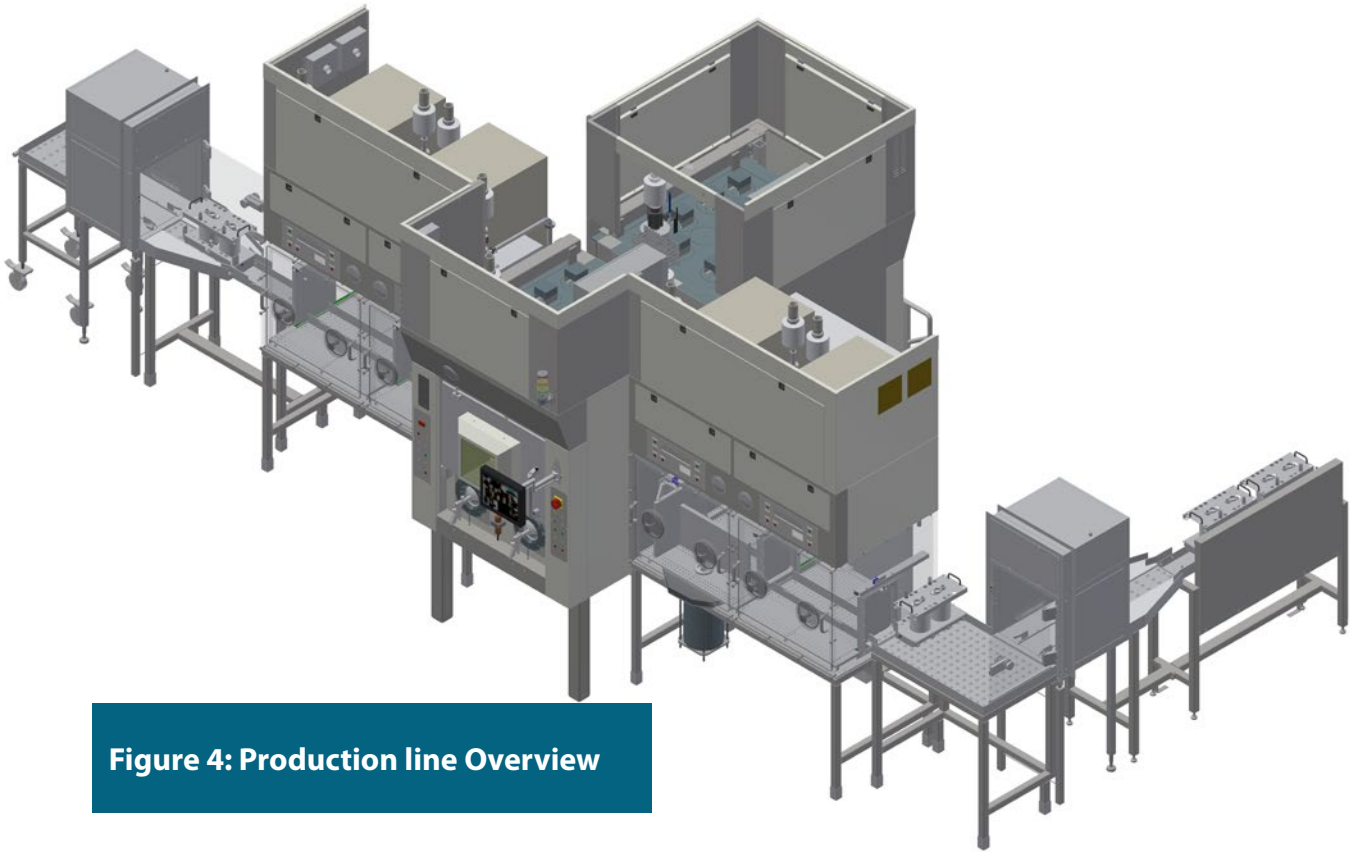

Figure 4: Production line Overview

Results

Among the technical advantages and GMP compliance with special clean room barriers and laminar flow modules this facility design is still cost effective. Even it offers the possibility for an installation at sites were only small areas are available. Furthermore an enhanced radiation protection is realized through abandonment of manual assembly steps at the already loaded generator. However the applied aseptic procedure is more time consuming than a simultaneous loading/sterilizing of multiple columns before their assembly into the generators.

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Annotation: Subject to change without notice

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