Ensuring quality while going local: IAEA helps Cuba produce radiopharmaceuticals

By Nicole Jawerth

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— René Leyva Montaña, Director of Production, CENTIS , Cuba

Cancer and cardiovascular disease are health conditions Cuba will now be able to more readily diagnose and treat thanks to its newly built facility for producing key radiopharmaceuticals. Nuclear medicine requires a constant and reliable supply of these radioactive drugs, prepared according to what the industry calls good manufacturing practices (GMP), and there have so far been limitations in getting them to the island nation.

"Through our work with the IAEA, we now have a dedicated GMP compliant facility and the expertise to meet most of our national needs for diagnostic and therapeutic radiopharmaceuticals for helping patients," said René Leyva Montaña, Director of Production at the Isotope Centre (CENTIS), Cuba's centre dedicated to radiopharmaceutical production.

The newly established facility for producing Y-90-based radiopharmaceuticals has good manufacturing practices compliant hot cells for protecting workers and ensuring the production of high-quality drugs.

(Photo: CENTIS)

GMP follow a series of international quality-assurance standards designed to protect patients from bad quality products. The standards outline the requirements to ensure that the pharmaceuticals produced are of a high quality, safe and effective, and that they contain the correct potency. "Becoming GMP compliant is a demanding, but important process, as a facility must be designed to ensure quality since the products have to be prepared already ready for patient use," said Joao Osso, Head of the Radioisotope Products and Radiation Technology Section at the IAEA.

Cuba's new facility will produce generator-based radiopharmaceuticals (see box) with yttrium-90 (Y-90), a key component in nuclear medicine to treat liver cancer and other conditions. Y-90 is produced from its parent isotope, strontium-90 (Sr-90). Sr-90 is a radioisotope, which means it is a radioactive element that decays towards stability. As it slowly decays, it releases Y-90, another radioisotope that has a much shorter decay time. Using special devices called generators, Y-90 can be 'milked' from the Sr-90 inside the generator. The Y-90 is then quickly purified and tagged to specific molecules to be used in nuclear medicine.

"Being able to produce the Y-90 generators in the country is much more economical and feasible than buying completed products abroad, as Y-90 has a short decay time, which makes it very difficult and costly to transport," said Osso, adding that Cuba will still need to buy raw materials, like the Sr-90, from suppliers abroad.

The IAEA has supported Cuba in developing the GMP compliant facility by providing the technical assistance and training needed for the development and production of Y-90, including labelling, quality control, metrology, safety and security, Osso said. Cuba has also received IAEA assistance and funding to buy analytical, radiological protection and metrology equipment and the materials required.

At this stage, CENTIS is preparing different formulations of Y-90 for diagnostic and therapeutic radiopharmaceuticals that can soon go to clinical trials and later to patients, explained Leyva Montaña. The facility is now waiting for the final licensing approval before it is ready for full-scale production, Leyva Montaña added.

Tackling an international supply problem

In contrast to Y-90 and Sr-90, which are widely available, technetium-99m (Tc-99m), another radioisotope of importance to Cuba and much of the world, is facing international supply problems due to production issues with its parent radioisotope, molybdenum-99 (Mo-99).

"Tc-99m is the 'workhorse' of nuclear medicine. Over 70 per cent of all nuclear medicine studies carried out all over the world use this single isotope," Leyva Montaña explained. Global supply problems with Tc-99m began in the late 2000s due to production stops by two nuclear reactors responsible for two-thirds of the world's supply of Mo-99. The challenges with these reactors and the limited production capabilities of other countries impact the availability of supplies, said Osso. Strict air transport regulations related to transporting radioactive material has also created challenges with moving international supplies particularly to islands such as Cuba, Leyva Montaña added.

"One of the main problems for Cuba that may arise from the supply issues is the price increase of Mo-99. As the prices go up, we would eventually not have the funds to import all that is needed, and consequently, patients would not receive the assistance they need," said Leyva Montaña. "Until now, though, the international supply problems have not had a significant effect on Cuba, but we expect there could be an impact so we are working on solutions now to try to mitigate that."

Cuba will soon have good manufacturing practices compliant facilities able to produce Mo-99/Tc-99m generators.
(Photo: CENTIS)

One of Cuba's approaches to mitigate supply challenges has been to collaborate with the IAEA in finding new suppliers of Mo-99, as well as to develop its own facilities to produce the Mo-99/Tc-99m generators, Leyva Montaña said, adding that the benefits will trickle down to other islands in the Caribbean. "The project will have a very positive impact on Cuba, and will also prepare Cuba to give the necessary support to small countries in the region."

Cuba's role in the region and internationally has changed since the country began collaborating with the IAEA, said Leyva Montaña. "First, it was Cuba requesting the support with fellowships and expert training, but now we are providing training to fellows in radiopharmaceuticals and generators production, supporting IAEA coordinated research projects, and facilitating exchanges and cooperation with several countries internationally."

THE SCIENCE

Radiopharmaceuticals

Radiopharmaceuticals are medical drugs that contain small amounts of radioactive substances called radioisotopes. Radioisotopes are atoms that emit radiation. The radioisotopes used in radiopharmaceuticals can be produced by irradiating a specific target inside a nuclear research reactor or in particle accelerators, such as cyclotrons. Once produced, the radioisotopes are tagged on to certain molecules based on biological characteristics, which then result in radiopharmaceuticals.

Once inside a patient's body, the different physical characteristics and biological properties of radiopharmaceuticals cause them to interact with or bind to different proteins or receptors. This in turn means that the drugs tend to concentrate more in specific body parts depending on that area's biological characteristics. Therefore, using special cameras, doctors are able to precisely target areas of the body to examine or treat by selecting specific types of radiopharmaceuticals. If the radioisotope emits particulate radiation the radiopharmaceutical may also be used in therapeutical applications.