EUROPEAN RADIOECOLOGY ALLIANCE

ALLIANCE Webinar: **Assessing impact of production, use and disposal of radiopharmaceuticals on members of public and the environment.**

2nd June 2022 – 9:30-16:30

SUMMARY OF THE WEBINAR

The webinar aimed at gathering information, including insight experiences from regulators, scientists, producers of radiopharmaceuticals (RPs) and experts in the field of nuclear medicine, necessary to carry out dose assessments for members of the public and non-human-biota. About 60 people (scientists working at universities and research centres for nuclear medicine, hospitals as well as in regulatory bodies) attended the webinar from all over the world.

The summary below gives an overview of facts that were presented and major statements from speakers.

Chiel Scholten from Netherlands presented the findings of the JRC study (published in 2021) on "Sustainable and Resilient Supply of Medical Radioisotopes in the EU" which focused on the market of therapeutic radionuclides (RN) (with new products such as ^{177}Lu-DOTATATE and ^{223}Ra-Cl2). In Europe, different radionuclides are being used or are under investigation for use for therapeutic purposes, e.g. ^{32}P, ^{47}Sc, ^{67}Cu, ^{89}Sr, ^{90}Y, ^{131}I, ^{153}Sm, ^{166}Er, ^{177}Lu, ^{186}Re, ^{211}At, ^{212}Pb, ^{213}Bi, ^{223}Ra, ^{225}Ac, ^{227}Th. The most used radionuclides are ^{131}I, ^{177}Lu and ^{90}Y with activity at time of administration reaching 50.000-250.000 GBq.

In the next 10 years, it is expected that the use of ^{177}Lu, ^{225}Ac, ^{227}Th and ^{166}Ho will increase and use of ^{90}Y, ^{169}Er as well as ^{131}I be stable. Nuclear reactors produce most of these radionuclides. At European level, in the past years, production and demand were stable and local suppliers were available. However, due to future increase in demand and shut down of some older nuclear reactors, the RN supply could become critical. Improvement of standardised national data on the use of RPs and widen information-sharing regarding supply capacities are two main recommendations from authors of the document for ensuring availability of the medical radioisotopes in the years to come.

Sampsa Kaijaluoto from Finland and Philipp Hartmann from Germany provided two examples of how proof of dose compliance with dose limits is carried out from a regulators' perspective. In particular, in both presentations the main challenge expressed is the recognition of the main exposure pathways for members of the public following the use of therapeutic radionuclides.

The Finnish study focussed on the external radiation from disposed diapers from patient treated at the hospital - with ^{131}I and ^{177}Lu - who come back at home and share space with relatives and caregivers. In this case, the dominant exposure situation (external irradiation) is for minors, which leads to doses higher the 0.1 mSv/y. A study is therefore planned to specify/set specific clearance values for excreta disposed in household waste.

The German study focused on the use of the alpha-emitter ^{227}Th for outpatient treatment. In this case, effective doses for members of the public were quantified conservatively and for most generic situation in Germany considering that the radionuclides leave the patient's body and enter the municipal sewage system. Additional releases may occur if patients die during or shortly after the medical therapy and their bodies are cremated. The potentially occurring doses are very low.

In Europe, the largest emitters of ^{131}I into the environment are the radiopharmaceutical production facilities (i.e. ^{123}I, ^{124}I, ^{125}I and ^{131}I), especially because of their size, i.e. only few companies produce the most of ^{131}I. Iodine is produced simultaneously with ^{99}Mo and ^{133}Xe using either fission of ^{235}U and neutron activation or neutron activation of stable target (e.g. ^{130}Te). Olivier Masson presented studies regarding monitoring of routine operations in Europe: significant discharges occur from medical isotope production facilities with authorisation limits up to several hundreds of GBq/y. These are much more relevant than releases from NPPs. In 2008 and 2011 there were two significant accidental releases of ^{131}I in Belgium (48 GBq) and in Hungary (342 GBq).

Geert Biermans from Belgium reported over a monitoring campaign to study behaviour of medical radionuclides and impact on workers of wastewater treatment plants carried out by FANC, Belgium. The monitoring campaign focussed on the presence of medical radionuclides at the inlet and outlet of wastewater treatment plants collecting liquid discharges from 5 major medical facilities in Belgium. The results indicate that in general concentrations in solids at the inlet fulfil the Belgian regulations with the exception of ^{131}I. In sludge and at the outlet of a WTP, ^{131}I was mainly found fixed to the dry matter, whereas for ^{99m}Tc it was not possible to draw similar conclusion. In general, no increase in ambient dose rate as well as no increase in radioactivity measured at the WPT outlet were found.

An increase in the amount of producing facilities and/or of different therapies, i.e. with different radionuclides, can affect the way regulatory provisions and monitoring activities need to be carried out. In fact, the dynamism with which new developments occur may cause a mismatch between how impact studies are carried out and how practical handling of the new therapies occurs. This is considered the main challenge from regulator's perspective in Belgium. In the future, focus on improvement of modelling of the releases (depending on type of medical treatment/radionuclide involved) and of the WTP system as well as on accounting for incidental scenarios is seen as necessary.

Jordi Vives i Batlle from Belgium provided more insight into the modelling issues: examples of assessments for planned and emergency releases related to medical radionuclides' production, application and final disposal is rather scarce. In particular, the environmental behaviour of novel radionuclides is poorly known, with limited or no transfer parameter data (e.g. ^{225}Ac, ^{177}Lu), the sewer system can be described with different level of complexity and detail and unusual exposure pathways may be considered. For pulsed discharges, dynamic models need to come into play.

For future development of methodologies for dose assessment, focus on scenarios including uncommon exposure pathways seems central, together with the improvement of monitoring programmes for targeting medical radionuclides, including measuring campaigns for quantifying model parameters. Missing knowledge of how radiopharmaceuticals distribute into the environment should also be analysed further since their physico-chemical form impacts mobility and bioavailability

in the environment. Overall, there is need for producing scientific guidance to regulators, i.e. providing information they need to have available for carrying out dose assessment.

Cinzia Pettinato from Italy presented the type of work she carries out at the Policlinico Hospital in Milan, where she is appointed as medical physicist and RPO. In particular, she has to evaluate clearance of solid waste material and liquid effluents following outpatients' treatments with medical radioisotopes. This includes the possible escape from radiometric control of some activity used in therapy. Calculations for solid waste are carried out based on NCRP Report No. 123 and dose limit is 10 microSv/y. The two publications ICRP 53 and ICRP 128 are considered, with which the total activity released into the sewer by hospital is quantified. Calculations for solid waste and liquid discharges indicate that releases are well below designated dose limit of 10 microSv/y. On the other hand, calculations for gaseous discharges indicate that such releases of gases in the atmosphere are not negligible in case an onsite cyclotron for PET applications is present at the site.

Veera Van Steen from Belgium described the activities related to waste management of irradiated targets for Mo-99 production at IRE. IRE produces ^{131}I and ^{177}Lu for radiotherapeutic purposes, focussing on the extraction of ^{99}Mo and its purification. Of the ^{99}Mo supply chain only the products ^{99}Mo, ^{133}Xe and ^{131}I are used whereas the other products are considered as waste. Different waste streams occur depending on the isotope mix, contamination level and type of waste (liquid, compactable, ..) and different evacuation (clearance) procedures are then necessary. The management of waste consists in various steps, i.e. avoiding and reducing waste in first instance, sorting the waste, treating the waste and characterising it via measurement. After waste is properly managed either clearance process/conditional evacuation occurs or preparation for transport and transfer to radioactive waste storage site takes place. To further reduce waste, an alternative ^{99}Mo production method is being developed by IRE in the SMART Project using an electron accelerator other than nuclear reactor neutrons and ^{100}Mo instead of a uranium target.

Similarly, **Marian Meckel from Germany** gave an overview on the production techniques and research activities at his company related to production of ^{225}Ac and ^{177}Lu, with the main goal to reduce impurities in the medical product.

CHAT QUESTIONS AND ANSWERS

From Wolfgang Wadsak (Europen Association of Nuclear Medicine) to everyone
Short remark: VISION trial regarding [177Lu]Lu-PSMA-617 is finished. Results were published in New England Journal of Medicine. FDA already approved marketing authorization a few weeks ago under the name of Pluvicto. EMA authorization to be expected this year as well. So, Lu-177 demand will further increase.

From Sampsa Kaijaluoto to everyone:
HERCA conducted a survey on 2019 on the use of therapeutic radionuclides. The data from that survey are going to be published in scientific article.

From Jila KARIMI DIBA (National Radiation Protection Department, Iran) **to Chiel Scholten:**
You export RD to countries not in Europe. What is your plan for the future when 5 reactors will stop operation?
The EU commission has to plan on this, currently no information about foregoing strategy is known to us.

From Klaus Schomäcker (University of Cologne, Clinic of nuclear medicine) to Geert Biermans:
You are speaking about exotic radionuclides with unknown behaviour in environment. Can you give us some examples?
Geert Biermans: If you google lutetium and environmental behaviours, there is very little available. When a new treatment starts, in the literature there is not much information. Sometimes there is only a single study and for regulators this is a problem
Jordi Vives i Batlle: He agrees with Geert. Very little information on some radionuclides e.g. lutetium (half-life not very long but not very short, very soluble in the environment)
Geert from regulation point of view it will be useful to make a database or a "sheet" with the information available on a specific RN (focused on information needed for dose assessments in the context of medical RNs)

From Sampsa Kaijaluoto to Geert Biermans:
Ir-192 is a surprising find in the monitoring activities. Can you guess its source?
Geert Biermans: Not sure where it comes from. Maybe a nuclide used in research, not necessarily is medical. FNAC does not know.

From Olivier MASSON To Geert Biermans:
Because incinerators are encouraged in WWTP both to reduce the volume of sludges or recover calories to dry the sludges or heating of the premises, did you look at possible secondary I-131 emission to the atmosphere?
Geert Biermans: emission to the atmosphere is possible, but is a "guess". Incinerators only admit big volumes for incineration. By that time the radioactivity may go down (radioactive decay). Emission from the waste treatment plant will be then low.

From David CELIER (IRSN, France) to Cinzia Pettinato:
What kind of bin controller is used? (dose rate, gamma spectrometry?)

No answer was recorded

From Sampsa Kaijaluoto to Cinzia Pettinato:
What is your experience with delay tanks? Do they significantly reduce (collective) radiation exposure? What about exposure of the workers that take care of decay tanks?
Cinzia Pettinato: They are not very important. Every medical nuclear facility needs to have decay tanks. However, not a lot of exposure is expected from these.

From Jolien Berlamont (FANC, Belgium) to Cinzia Pettinato:
Is Lu-177 used in Italy and don't you require hospitalisation for those patients (24h) due to the fast excretion phase?
Cinzia Pettinato: With the new Italian regulation we are not obliged to have the patients in the hospital. It can be a problem if there are a lot of patients treated with Lu-177 (usually they need to stay in hospital because of other clinical problems not because of radiological problems).

From Jila KARIMI DIBA to everyone:
IAEA TECDOC-1714 provides good information regarding delay or decay tank.

From David CELIER (IRSN, France) to everyone:
about decay tanks, Irish authority also published an interesting study in 2010 (https://inis.iaea.org/search/search.aspx?orig_q=RN:43091818)

From Klaus Schomäcker to everyone:
Any idea how much Tc-99 is released into the environment through the decay of Tc-99m? What is the behaviour in the environment.
Jordi Vives i Batlle: I don’t know how much Tc-99 appears in the environment specifically from Tc-99m decay, but this element is environmentally important. Tc-99 can bioaccumulate in hepatopancreas and green glands of crustaceans. It is one radionuclide that you will typically look for in an environmental impact assessment.

From Peter Covens (Vrije Universiteit Brussel, Belgium) to everyone:
The Lu-177m issue will be an end of story in the (near) future

From David CELIER to Peter Covens: for Lu177-PSMA yes, but will it be the same for Lutathera?

From Peter Covens to everyone:
@David Celier: Yes, that is what I heard. Novartis will go for the No Carrier Added (nca) version

From Peter Covens to everyone:
The Tc-99 amount is simply the ratio of the half-lives of Tc-99m and Tc-99

From David CELIER to everyone:
I'm not a specialist on this subject, but I think Tc99 behaviour is quite well known because of discharge of nuclear fuel reprocessing plants

From Bogusław Michalik (GIG, Poland) to everyone:

Tc-99 is the great absentee .... or I've missed something

From Peter Covens to everyone:
Very interesting webinar!!!

From Eva Kabai (BfS, Germany) to Philipp Hartmann:
Which radionuclides you considered for the dose estimations: Th-227->Ra-223->Rn-219-> or also Po-215?
Laura answers on behalf of Philipp: Dose calculations included Th-227 and Ra-223, after that the half-life is very short.

From Wolfgang Wadsak (EANM) to Philipp Hartmann:
Did you also make calculations for more realistic scenarios - not only worst-cases? What would be a realistic factor going from worst-case to realistic exposure scenarios?
Laura: There were no realistic scenarios considered. The main goal was to consider parameters and assumptions valid for all regions in Germany. They were very conservative in their evaluation (this is enough for them).

From Laura Urso to Marian Meckel:
Does the amount of impurity obtained during RN production go 1:1 into the medical product? If so, what is the acceptable % of impurity? Is this based on dose assessment for members of the public and/or Clearance levels?

From Wolfgang Wadsak to everyone:
@Laura: that depends on the chemistry. If RN from different elements, normally radiochemistry will not allow an incorporation into molecules in similar ratios but rather favour the wanted RN over the impurities. Different stories if you look at RN from the same element. Then everything stays in. Acceptable levels of impurities are determined in the monographs of the Pharmacopoeias. This takes unwanted doses to the treated patient into account from uptake and retention in critical organs.

From Thomas Onumah to everyone: what is the specific behaviour of radionuclide in the ecosystem? please I want more information to assist me in my Mphil research work. I intend researching in such an area.
Jordi Vives i Batlle: different RNs have different behaviours. It also depends on the ecosystem considered: e.g. in aquatic ecosystem it is important if they are soluble or not, governed by the K_d. IAEA handbook on transfer parameters (report of 472) is recommended.

From Laura Urso to Veerle Van Steen: to what extent the circular economy comes into your cost assessment- e.g. recycling?
Veerle Van Steen: it is indeed central.

From Peter Covens to everyone:
What is the fraction combustible/non-combustible in solid waste @IRE?
Veerle Van Steen: it is about 2-3 times more combustible than no combustible

From Thomas Onumah to everyone:
Can we have access to the slides after the program?
Laura: Slides will be made available, either on ALLIANCE website (public) or per E-mail to all participants

Two questions remain unanswered:
From Bogusław Michalik to everyone:
Using Ra-226 for Ac-225 production, what must be the purity (content) of radium in irradiated target?

From Peter Covens to everyone:
Can both methods (p,2n) and (y,n) on Ra-226 really exclude Ac-227? Somewhere in the production process there will be some neutron thermalisation that can lead to Ra-227 -> Ac-227

From Jila KARIMI DIBA to everyone:
So many thanks for very productive and fruitful webinar. Special thank to Ms. Laura. Very well managed

From Simon O'Toole (EPA, Ireland) to everyone:
Thanks to all the presenters and organisers for an excellent webinar.

From Jolien Berlamont to everyone:
thank you for this very nice and interesting webinar!

Many others also wrote Thanks!