GE Healthcare Comments on the European Commission Proposal
In Preparation of a Legal Proposal to Combat Counterfeit Medicines for Human Use

Introduction

GE Healthcare is broadly supportive of the initiatives proposed by the European Commission to act to protect European patients in the areas described in the Commission proposals. GE Healthcare (GEHC) is a global manufacturer of radiopharmaceuticals and contrast agents, and healthcare medical imaging and information technologies and equipment. GEHC has manufactured and supplied radiopharmaceuticals for more than 50 years and it is in relation to proposals for enhanced traceability of batches throughout the supply chain (so-called pedigree) that GEHC would like to comment, specifically in relation to radiopharmaceuticals.

Radiopharmaceuticals and their Transport and Distribution

Radiopharmaceuticals are radioactive drugs (any medicinal product which, when ready for use, contains one or more radionuclides (radioactive isotopes) included for a medicinal purpose). (1). They are most often supplied in injectable forms, that are used in nuclear medicine procedures to diagnose and/or treat diseases such as cancer, cardiovascular disease, and neurological disorders. They are typically distributed directly to hospitals and physicians who perform nuclear medicine procedures, typically packaged as finished individual or multiple doses ready for injection.

A further type of radiopharmaceutical is a radioactive generator such as a molybdenum Mo99/technetium Tc-99m generator; these are shipped to a hospital nuclear medicine department, radiopharmacy or licensed healthcare professional. The eluate from the generator Tc-99m is used to reconstitute a non-radioactive kit; this becomes the final dose for the patient. The kits are also shipped from the manufacturer.

Because radioactive radiopharmaceuticals are used in patients to diagnose, rather than treat disease, they have very short shelf-lives. In contrast to shelf-lives of conventional drugs, which are measured in years and months, radiopharmaceutical shelf-lives typically range from several hours to several days. Therefore, these products must be shipped rapidly from their place of manufacture to the end user (hospital, nuclear pharmacy, qualified healthcare professional or commercial imaging facility).

The packaging and transport of radioactive medicinal products is regulated by National and International regulations for the safe transport of radioactive material.

Oversight over Radiopharmaceutical Distribution

In addition to meeting pharmaceutical GMP and GDP regulations, radiopharmaceutical manufacturers must be licensed by a Nuclear regulatory authority. In order to obtain a licence, the manufacturer must demonstrate that its facilities are adequate to protect health and minimise danger to life or property, that it is qualified to use radioactive material, that it has established a radiation protection program, and that it has established controls and procedures for management, record keeping, accounting, management review, and control and use of radioactive materials.

A hospital radiopharmacy or imaging facility that receives radiopharmaceuticals from a manufacturer and prepares them in patient-specific doses must also be licensed to receive

radioactive material by the appropriate national licensing authority for each type of radiopharmaceutical it handles. Like the manufacturer, a hospital, imaging facility or nuclear pharmacy is subject to detailed requirements for safety controls and procedures.
Among the extensive licensing requirements imposed on manufacturers and recipients of radiopharmaceuticals are those relating to the transport of radiopharmaceuticals. A manufacturer is prohibited from shipping a radiopharmaceutical unless it first verifies that the recipient's licence authorises the receipt of the type, form, and quantity of the radiopharmaceutical that is to be transferred.

The manufacturer must maintain a record of each transfer of a radiopharmaceutical to a customer following the shipment. Due to the nature of the material, the manufacturer has a duty of care to ensure the recipient knows exactly what is being sent. On receipt the receiver must ensure that the correct packages are received and accounted for.

Unlike the transport of conventional pharmaceuticals, the shipment of a radiopharmaceutical between manufacturer and end user is regulated by national and international regulations for the safe transport of radioactive material. In addition to meeting packaging, labelling, and marking requirements and the placarding of the vehicle, the manufacturers must provide the carrier with shipping papers that identify the name of each radionuclide in the shipment, a description of the physical and chemical form of the material, and the activity contained in each package. The papers for each shipment must be retained by the manufacturer for three years and provided to authorised government or regulatory authority officials on request.

These controls ensure that a radiopharmaceutical manufacturer can only ship products to a known, licensed healthcare professional, hospital, nuclear pharmacy or imaging facility and no one else. The radiopharmacy or receiving facility must then confirm that each shipment received was ordered through proper channels, has proper shipping papers, and contains the products described in the papers. Under this rigorous system, the receipt of diverted or counterfeit radiopharmaceuticals is extremely unlikely. For this reason alone, an additional system of standard identifiers, tracking and tracing, and authentication would be redundant and unnecessary.

Radioactive Radiopharmaceuticals Do Not Face a Realistic Risk of Counterfeiting

Radioactive radiopharmaceuticals are extremely difficult to counterfeit and are not prescribed to or used by individuals without medical supervision. Non radioactive counterfeits would immediately be recognised and would be ineffective. To make a radioactive copy of a radiopharmaceutical a would-be counterfeiter would need access to the relevant isotopes.

The radionuclide active pharmaceutical ingredients (API) used in these products are generally obtained as by-products from nuclear reactors or created using particle accelerators. A would-be counterfeiter could not conceivably build his own reactor or accelerator and escape detection, even if the expense were not prohibitive. Instead, he would have to obtain API from one of a handful of reactors or accelerators in the world that produce such products, which are highly regulated and subject to strict registration, licensing, and distribution restrictions of their own, including requirements for verifying the authority of the ordering entity to receive shipment. Even if obtaining the necessary radionuclide raw materials were possible, their high cost would be prohibitive for a counterfeiter. For reactor by-product based and accelerator-

based products alike, the risks of radiation exposure, the high cost of specialised equipment and radiation protection systems necessary to make finished product, and the risk of enforcement by the regulator would make counterfeiting both undesirably risky and financially impractical.

Finally, the radioactivity which constitutes the active pharmaceutical ingredient in a radiopharmaceutical is constantly decaying; hence these products require rapid, direct shipment, without wholesalers or other intermediaries. Because of the very short shelf-lives of radiopharmaceuticals the loss in radioactivity in any delayed or diverted product would be immediately discovered on receipt by the end user.

Conclusion

We understand that, in general, standardised numerical identifiers and electronic pedigree and track and trace systems would serve an important public health policy of protecting patients from counterfeit and diverted drugs. However, we believe that, because of the unique features of radiopharmaceuticals and their distribution as described above, these products do not present the same concerns in this regard as conventional, non- radioactive drugs. Therefore, radiopharmaceuticals should not be subject to standards and requirements for standardised numerical identifiers, tracking and tracing systems, and electronic pedigrees.

About GE Healthcare
GE Healthcare provides medical imaging and information technologies, medical diagnostics (contrast agents and radiopharmaceuticals), patient monitoring systems, drug discovery and biopharmaceutical manufacturing. Headquartered in the United Kingdom, GE Healthcare is a $17 billion unit of General Electric Company (NYSE:GE). Worldwide, GE Healthcare employs more than 46,000 people in more than 100 countries.
Website: www.gehealthcare.com**.**

1. Directive 2001/83/EC Article 1 (6)

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