NUCLEAR MEDICINE'S DOUBLE HAZARD
Imperiled Treatment and the Risk of Terrorism

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This article examines the production of metastable technetium-99 (Tc-99m), the world's most important radiopharmaceutical, focusing on reliability of supply and risks of nuclear terrorism. Only four producers manufactured about 95 percent of the world's Tc-99m; a closure of any of them could cause worldwide shortfalls. Moreover, all four employ highly enriched uranium in their production process, in a form relatively easy to convert into the metal needed for a nuclear bomb. The technology to employ low-enriched uranium (LEU)—not usable in weapons—to produce Tc-99m is proven, available, and has been used by smaller producers. However, political determination and sufficient funding are needed to convert the major producers' isotope production to LEU and encourage new LEU-based production. Such efforts are needed to ensure supplies and reduce security risks.

KEYWORDS: Nuclear terrorism; highly enriched uranium; low-enriched uranium; nuclear reactor; molybdenum-99; technetium-99m; medical isotopes

The most important isotope used in nuclear medicine today, metastable technetium-99 (Tc-99m), the daughter product of molybdenum-99 (Mo-99), is primarily supplied on a worldwide commercial basis by just four producers, all of which rely on a small number of nuclear research reactors that use highly enriched uranium (HEU) targets to produce Tc-99m. This state of affairs is potentially hazardous for two critical reasons. First, medical patients are now dependent on too few nuclear reactors, with too great a risk that shutdowns could result in cancellations of lifesaving treatments. Second, HEU target material can be used to fabricate a nuclear bomb. The technology to produce Mo-99 using low-enriched uranium (LEU) targets is proven, available, and has been used routinely by two smaller producers for a number of years (moreover, other non-HEU production technologies also exist). However, political determination and financial support to convert the major producers' isotope production to LEU has been lacking. There are currently no commercial incentives for lead producers to convert from HEU use. Though the market for radioisotopes is expanding rapidly, with new production capacities needed to ensure radioisotope supply, high up-front costs, low profit margins, and difficult licensing processes mean that the establishment of new facilities is extremely difficult without government intervention. Meanwhile, policies related to HEU conversion and medical isotope production have wavered over the years. A new political commitment to support increased Mo-99 production without the use of HEU is essential. Otherwise the general public will continue to face a double hazard: insufficient future supplies for medical treatment along with the possibility of nuclear terrorism.

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This article first reviews the main uses of Tc-99m before turning to a history of its production, including past efforts to ensure a reliable medical isotope supply. Next, it examines broader policies enacted to reduce the use of HEU and these policies' influence on medical isotope production, with a particular focus on U.S. legislation related to HEU exports and on programs aimed at converting Mo-99 production from HEU to LEU and producing Mo-99 without the use of nuclear targets. It concludes with a review of current policy and activities in this area and suggests measures to ensure supplies and reduce future risks.

The risks inherent in the current system of isotope production became particularly apparent in 2007, after revelations of operating license violations and security breaches at isotope production reactors in Canada and South Africa. The prolonged November–December 2007 shutdown of Canada's National Research Universal (NRU) reactor—triggered when it was discovered that two emergency pumps were not attached to emergency power supplies, as required by its operating license—dramatically reduced Tc-99m supply throughout North America. Production resumed only after the Canadian parliament countermanded Canada's nuclear safety commission.[1] In addition to questions about nuclear safety in Canada, this countermand focused concerns on the world's overwhelming reliance on a single Canadian reactor for medical isotopes. It also sent a dangerous message to other countries regarding regulation of their own nuclear facilities. Grant Malkoske, vice president of the Canadian company MDS Nordion, the world's largest producer of Tc-99m, reportedly had warned officials before the crisis erupted that in the event of a prolonged shutdown of the Canadian reactor, "we could see a global supply shortage of 30 percent."[2]

Another recent incident, the November 8, 2007 break-in at South Africa's Pelindaba facility, which also produces Mo-99 and has large supplies of HEU stored on-site, raised new questions about the security of that facility and the potential vulnerability of the weapon-grade material stored there. Armed attackers approached the facility from two sides; one group, able to defeat the facility's security system, entered the main emergency control room.[3] Even though the attackers were apparently after computers, not uranium, the incident is disturbing when one considers that Pelindaba houses enough HEU to create multiple bombs. Therefore, any security breach should raise concerns—and this was the second reported breach at the site in the past couple of years.[4] Further, as the supplier of some 15 percent of the world's Tc-99m, the secure and reliable operation of the SAFARI-I reactor at Pelindaba is critical to the world supply of this radioisotope.

Nuclear Medicine's Workhorse

Radioisotopes have important medical, scientific, and industrial purposes. The most widely used of these isotopes is Mo-99, which is used to produce Tc-99m, which is employed in some 30 million medical diagnostic procedures worldwide every year—80 percent of all nuclear medical procedures.[5] There are more than a hundred different such procedures in nuclear medicine—to determine the severity of heart disease, the spread of cancer, and the diagnosis of brain disorders—about 70 percent of which rely on Mo-99.[6] Tc-99m is recovered from generators at clinics and laboratories, which receive them from radiopharmaceutical suppliers.[7] Because the half-life of Mo-99 is just sixty-six hours, the useful lifespan of a Tc-99m generator is about one week. Thus a constant and reliable supply of Mo-99 is critical for nuclear medicine.[8]

At present, most production of Mo-99 takes place in nuclear reactors where a "target" (i.e., a special fuel element) made of enriched uranium is irradiated in a high flux area of the reactor.[9] The target is then dissolved in either nitric acid or alkaline solutions for one to three hours, after which the Mo-99 can be recovered and purified by a variety of processes. The Mo-99 is then sent to the manufacturer of Tc-99m generators, who must then quickly forward equipment to hospitals and other users.[10]

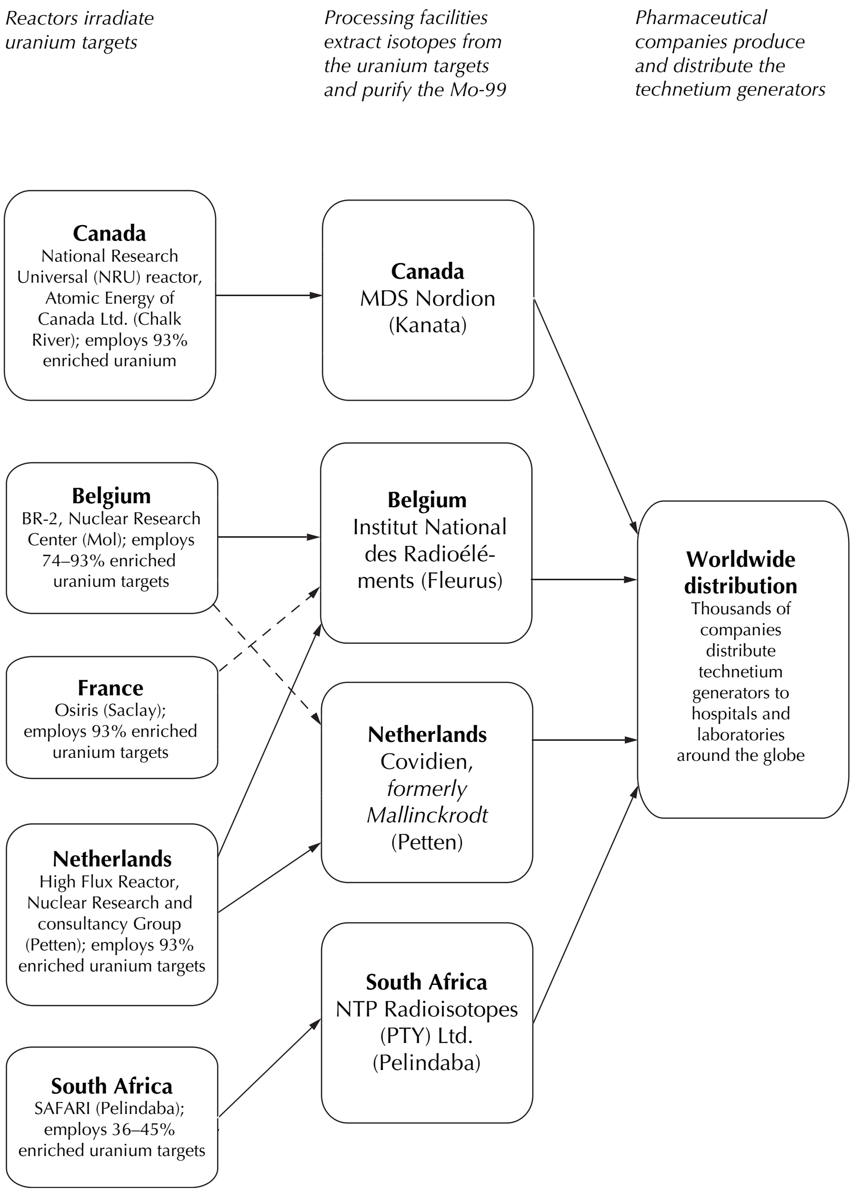
Nuclear Isotope Production Facilities and Risks

The amount of HEU used for medical isotope production was relatively small twenty-five years ago (in both absolute terms and as a percentage of all HEU in civilian use), when the Reduced Enrichment for Research and Test Reactors (RERTR) program to reduce use of HEU in the civilian sphere was initiated. Today, however, the amount of HEU used in targets for Mo-99 production is an increasing proportion of all HEU uses and is projected by some to increase to half of the HEU in civilian use by 2020 (assuming present trends and no conversion to LEU by the major Mo-99 producers).[11]

Mo-99 is currently produced in at least nineteen countries, with the largest four producers located in the European Union, Canada, and South Africa (see Figure 1). More than 90 percent of the world's supply of medical isotopes comes from MDS Nordion (Canada, using the NRU reactor), Covidien (formerly Mallinckrodt, using reactors in Belgium and the Netherlands), Institut National des Radioéléments (IRE, using multiple European reactors), and NTP Radioisotopes (Pty) Ltd. (South Africa, using the SAFARI reactor). Only Australia and Argentina rely on LEU targets for isotope production; while Argentina's production is small, Australia intends to become a large-scale producer within the next few years (see Figure 2). In addition, countries like India and China engage in small-scale production through neutron activation (without the use of uranium targets), mostly for local users (see Figure 3). However, all of the world's largest producers currently rely upon HEU targets in their isotope production programs (the enrichment level of targets varies from 36–45 percent in South Africa, to about 93 percent in Canada).

Although the quantity of HEU employed to produce Mo-99 was initially quite small, in 2007 the amount of uranium-235 (U-235) used by the world's four main Mo-99 producers totaled about 50 kilograms (kg), a quantity sufficient to produce two nuclear bombs. This contrasts with about 750 kg presently used worldwide to refuel research reactors, although this latter number has been decreasing each year, while there have been no decreases in the amount of HEU used for target production. If current estimates by U.S. Department of Energy (DOE) officials with the RERTR program prove to be correct and new fuel types allowing conversion of many research reactors are available in 2014, then soon afterward half of the HEU in use in reactors worldwide may be in fission targets for radioisotope production (if reactors are converted or shut down while HEU-based isotope production continues at full capacity). Moreover, many of the reactors currently used to produce isotopes are reaching the end of their service lives. Thus, key decisions on

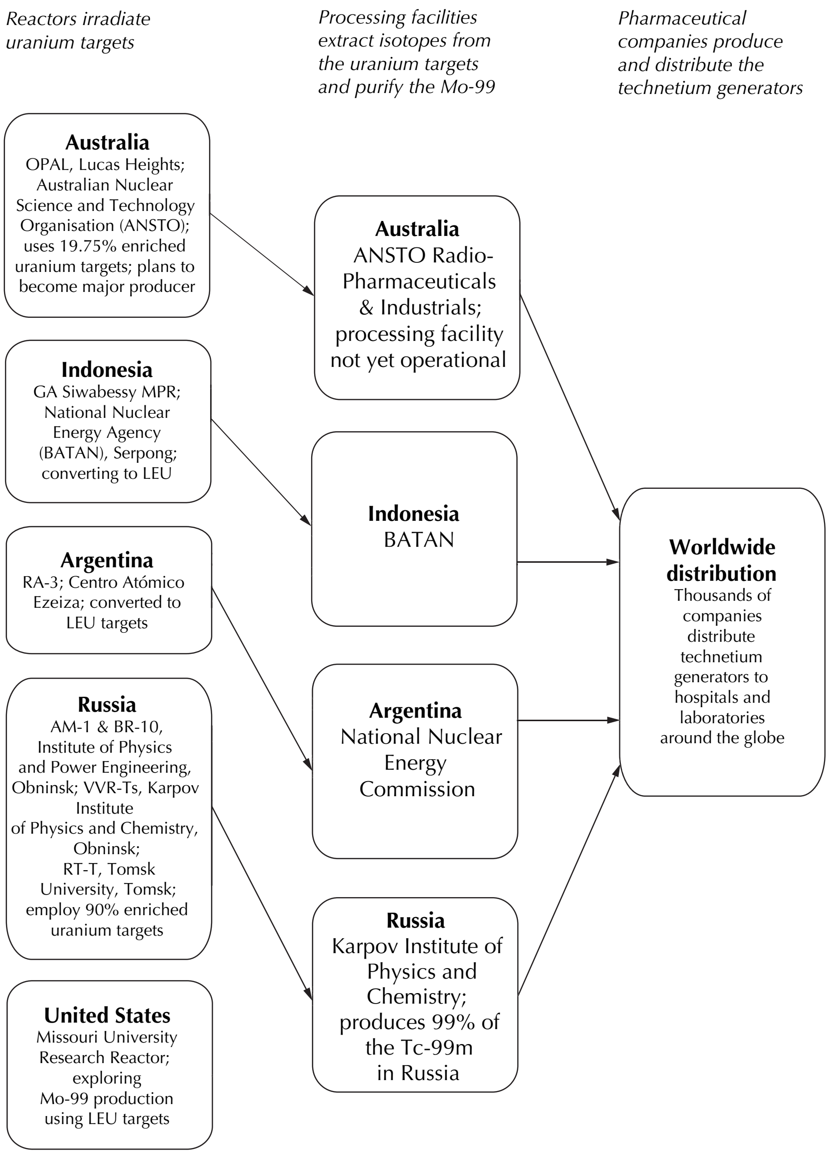
FIGURE 1
Major isotope producers



investments in new reactor and processing capacities will have to be made within the next few years.[12]

HEU targets used in Mo-99 production pose particular risks that make conversion of this production to LEU particularly important. Because of the relatively short time targets

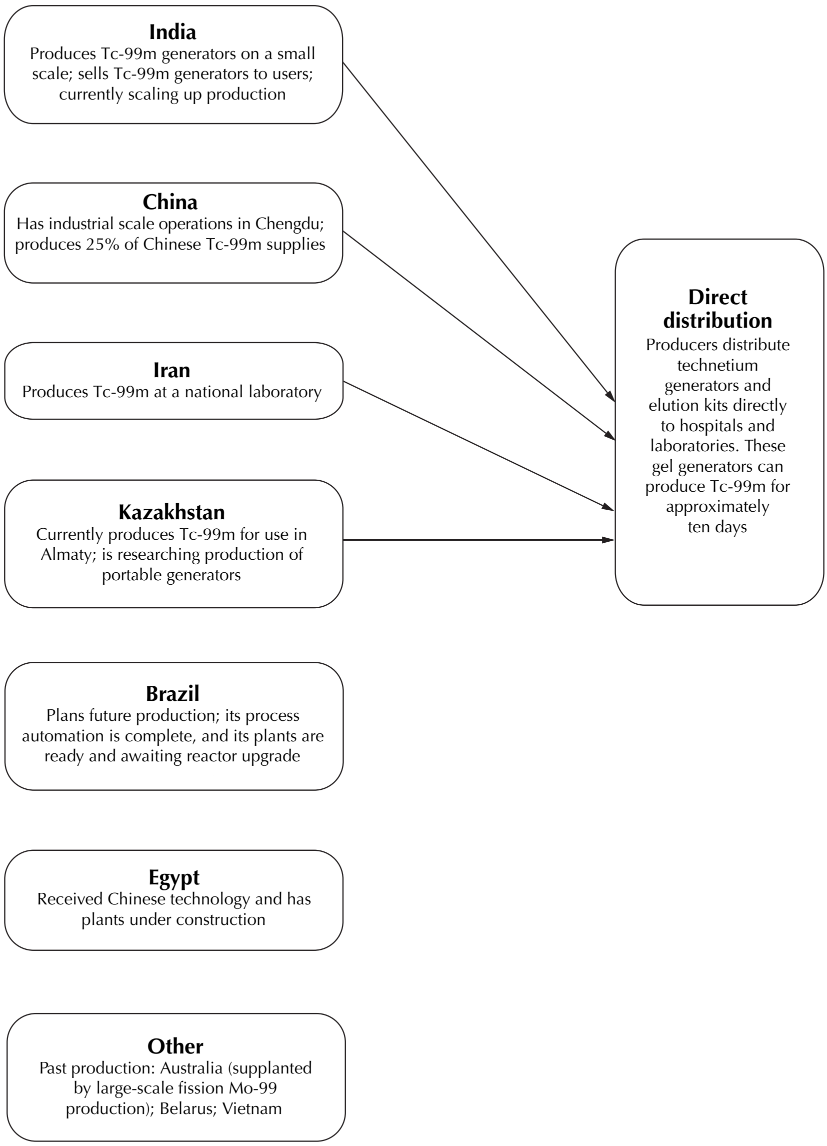
FIGURE 2
Selected other isotope producers (fission)



remain in a reactor (low burnup), the U-235 content of a spent 93 percent U-235 target is still above 90 percent HEU. Furthermore, because the target waste is in liquid form (acid dissolution) and in solid form as hydrated uranium oxide solid (alkaline digestion), it can be relatively easily converted into HEU metal (the material used in the production of a gun-type nuclear explosive device) via well-known chemical processes. And finally, short

FIGURE 3
Other isotope producers: neutron activation (gel generators)

Regional distribution from non-centralized production to meet local needs



irradiation time means that targets are not as "self-protecting" (highly radioactive) as spent reactor fuel.

Currently, security standards in most nations are based on worker safety regulations that consider the health effects of longtime exposure to nuclear materials in the workplace. For a worker in a Mo-99 generator production facility, the large volumes of target waste are sufficiently radioactive to be dangerous (and are therefore considered "self-protecting"). However, for a terrorist wishing to obtain enough HEU for a single weapon, the target waste can be contact-handled (and converted into uranium metal) without shielding after a cooling period of just three years, exposing the perpetrator to doses hazardous to long-term health but not sufficient to disable the person handling the material, a recent Argonne National Laboratory study indicates. In this scenario, only relatively small amounts of target waste (some 80 grams) need be handled at any one time; once each such batch is converted to metal (using the well-known PUREX process, which chemistry graduate students should be capable of handling), it can be stored while the next batch is processed.[13] The study notes:

> Considering that 5–8 million millirem (mrem) are required to cause immediate disorientation and coma in seconds or minutes, the received dose for removal of large quantities of this material would not be consequential to a dedicated terrorist. Converting this material to a weapon would not require elaborate shielding and could be performed in a garage with minimal dose to the processors.[14]

This dose rate is much lower than that produced by spent research reactor fuel. The Argonne report cites a dose rate of about 40 mrem per hour per gram of initial uranium for a spent HEU material test reactor fuel element burned to 60 percent (measured at 1 meter per gram of uranium), and concludes that because of its greater U-235 fraction (approximately 92 percent) and its lower dose rate, spent HEU target material is a far greater security and safeguards concern than spent research reactor fuel.[15]

Thanks to the success of the various Global Threat Reduction Initiative programs, the amount of HEU used for isotope production has become a relatively greater proportion of the HEU in use in the civilian sphere.[16] Unfortunately, there are already hundreds of kilograms of target waste containing only slightly irradiated HEU, resulting in a greater quantity of HEU stored at these processing facilities than is held at the majority of research reactors.

Storage and processing of HEU target waste poses safety as well as security problems. For example, because Canada's facility for this liquid waste is full, its operators have conducted criticality studies to ensure that storage could be reconfigured to accommodate additional material or that some waste could be removed and immobilized in concrete to reduce overfill. Of course, the immobilized material will eventually have to be removed from the concrete in order to downblend it for long-term storage—not a simple process. Waste storage space is problematic for other radioisotope producers, too. For example, like Nordion, the Mallinckrodt medical company (now Covidien) had intended to send its target waste to the Dounreay reprocessing facility in Scotland, before Dounreay was suddenly shut down in 1998. European plans still call for recycling of HEU target waste for production of new targets; while such plans will cut down on HEU in storage, it is not clear that this recycling will occur on-site. If not, the HEU will have to be taken to a facility for recycling and transported back to the reactor—adding yet another site of concern, along with increasing transportation (nuclear materials are generally considered to be most vulnerable during transport, where fewer security measures are usually available than at fixed facilities).

Reducing the overall volume of target waste in storage has tangible security benefits, but complete elimination of the HEU is a much more reliable option. As far as the author is aware, the only security upgrades at Mo-99 production reactors since September 11, 2001, have been at the BR-2 reactor in Belgium, and even there security may be strong for a civilian site but not when compared to military facilities. Security at isotope irradiation and production facilities around the globe was not designed to prevent terrorist attacks or the theft of materials for the construction of an improvised nuclear device (IND). Indeed, few countries have updated their security requirements sufficiently since 9/11.[17]

On the whole, requirements should be updated to include consideration of new threats, and the concept of "self-protection" of nuclear materials should be revised to reflect the amount of radiation required to incapatate would-be thieves (such a change is under way in the United States). These new requirements should include more nuanced recommendations than those in the current International Atomic Energy Agency (IAEA) guidelines on the physical protection of nuclear material and nuclear facilities.[18] Security requirements for nuclear power plants are insufficient for Mo-99 production, given that the material at the latter facilities is weapon-grade; requirements for protecting most spent research reactor fuel are similarly not enough, given the much lower levels of radioactivity found in irradiated targets. In short, sites handling HEU targets for Mo-99 production should have the same level of protection as materials at military facilities, because they too can be used to create a nuclear weapon.

Ensuring Mo-99 Supplies

The United States was the first producer of Mo-99 and continues to be the world's largest user of Tc-99m. Concerns over maintaining a sufficient and reliable supply of this isotope have been voiced since the late 1960s, soon after the discovery of Tc-99m and its applications. As new uses for this radioisotope continue to be discovered, and its use spreads rapidly throughout the world, the difficulty of ensuring adequate supplies of Tc-99m is likely to increase. The following section reviews the history of Mo-99 generator production and early efforts to ensure supplies to U.S. users.

The discovery that Mo-99 could generate Tc-99m was made by accident at Brookhaven National Laboratory in 1958 during experiments involving another isotope. The use of technetium as a medical tracer was first put forward by a Brookhaven scientist, Powell Richards, at the International Electronic and Nuclear Symposium in Rome in June 1960. Richards also promoted its use to the University of Chicago, which developed many medical procedures using Tc-99m in the 1960s. The half-life of Tc-99m is six hours—long enough for a medical examination, but short enough to avoid radiation damage to bodily organs. Mo-99, on the other hand, has a half-life of sixty-six hours, making it possible to transport over fairly long distances.[19]

Mo-99 was initially produced by the Atomic Energy Commission at the Brookhaven and Oak Ridge National Laboratories, but by 1966 the national laboratories could no longer keep up with the demand for Tc-99m generators and withdrew from production and distribution, letting commercial enterprises take over. The first commercial generator was produced by Nuclear Consultants, Inc. of St. Louis (later taken over by Mallinckrodt), and Union Carbide Nuclear Corporation, New York.[20] Production also began in Canada: on May 1, 1970 at the NRU reactor, and on May 1, 1971 at the Nuclear Research Experimental (NRX) reactor, both at Atomic Energy of Canada Limited's Chalk River Laboratories in Ontario.[21]

One reactor used for Mo-99 production in Pleasanton, California, was decommissioned in 1977, and Union Carbide's successor, Cintichem, closed the other reactor in Tuxedo, New York, in 1990. These shutdowns, together with the final closure of Canada's NRX reactor in 1992, meant that all of North America became dependent on Canada's NRU reactor for its Mo-99. Already in 1990, the U.S. Congress had established the Isotope Production and Distribution Program (IPDP), combining all DOE isotope production activities. This IPDP was also "responsible for ensuring a stable supply of Mo-99 to the U.S. medical community."[22] But the risks of relying on a single reactor for this supply led to a U.S. study, supported by a $250,000 grant from the radiopharmaceutical industry, to locate an alternative U.S. reactor to produce the isotope.[23] The perceived need to find a new source of Mo-99 was heightened by a brief strike in 1991 at the Canadian plant that processed Mo-99, which focused attention on the hazard of relying on a single source for Mo-99. The U.S. study eventually identified the underutilized Omega West reactor at Los Alamos National Laboratory, leading to plans to produce enough Mo-99 at Omega West to meet about 30 percent of the U.S. demand beginning in 1993.[24] DOE bought the Cintichem technology, and the government invested $3.5 million for process development at Los Alamos. However, a leaking coolant pipe was discovered in December 1992, provoking the DOE's Defense Programs division to announce that it would stop using the reactor. The IPDP, which was required by law to operate on a commercially viable basis, would have been forced to cover all operating costs.[25] But the Omega West cooling system was never repaired, and the reactor was instead shut down.

In the meantime, major U.S. radioisotope users concluded long-term contracts with other suppliers, particularly Canada's MDS Nordion, further reducing IPDP's commercial prospects. In 1996, the Annular Core Research Reactor (ACRR) at the Sandia National Laboratories in New Mexico was identified as an alternative Mo-99 producer (with potential to supply up to 70 percent of the U.S. market and 100 percent of the demand for short periods of time).[26] The decision to establish Mo-99 production at ACRR was made after completion of an environmental impact statement and, according to a 1996 news release from Sandia, after "Congress requested that DOE develop a reliable domestic source of moly-99."[27] Although the ACRR was converted for full-time isotope production and modifications to its associated hot cell facility were nearly completed, production never started. Buyers' needs were by then already being met by alternate producers, so the commercial success of the Sandia reactor seemed quite doubtful.[28]

Through the years, concerns over U.S. reliance on Canada's NRU reactor have waxed and waned, increasing temporarily whenever Canadian deliveries were threatened. In April 1995, for example, the NRU reactor suffered an unplanned four-day shutdown. While European sources were temporarily able to increase production enough to cover European demand normally supplied by Nordion, and while Nordion still met U.S. demand during this brief period, DOE indicated that the United States would have faced shortages had the Canadian reactor remained out of service for only one or two more days.[29] A mutual back-up agreement linking Nordion with Belgium's IRE stipulated that IRE would supply Nordion with the excess capacity of its facility for up to eight weeks in the event of a shutdown.[30] However, such excess capacity has proven insufficient. The November–December 2007 NRU shutdown reduced Tc-99m supply throughout North America, affecting both customers directly supplied by Nordion and those receiving Tc-99m generators from Covidien.[31] The *Journal of Nuclear Medicine* reported that for each month of disrupted supply, 50,000–90,000 patients in Canada and as many as 200,000 patients in the United States would be affected.[32] Nordion Vice President Grant Malkoske, similarly, has said that if the NRU reactor goes down for more than seven days, the other reactors cannot fully supply hospitals. When the other reactors did "ramp up" last winter, there was still a 35 percent global shortage, he noted.[33] Obtaining back-up supplies from other producers requires planning ahead to buy irradiation time at other reactors and prepare staff at alternate production facilities to ramp up production. While unplanned outages will thus remain problematic unless additional facilities are brought online, better planning is also necessary to ensure reactor shutdowns are coordinated and all capacities are put to good use.[34]

Though Canada's NRU reactor was again functioning by the end of December 2007 and will be fitted with required safety pumps, it is fifty years old and will eventually have to be shut down. Atomic Energy of Canada Limited (AECL) and MDS Nordion signed agreements in 1996 for the design and construction of two Multipurpose Applied Physics Lattice Experiment reactors, called MAPLE-1 and MAPLE-2, and a New Processing Facility (NPF) to replace the NRU reactor and its associated processing facility. Although the MAPLEs were supposed to be online by 1999 and 2000, the reactors were never finished and the project was abandoned in 2008.[35]

The dependence of North American consumers on Canadian isotope production was somewhat ameliorated by the entry of European producers into the North American market. In 1997, Mallinckrodt received FDA approval to use Mo-99 manufactured at the Petten reactor in the Netherlands for some of its U.S. radiopharmaceutical products.[36] Belgium's IRE similarly sells its Tc-99m generators in the United States today, as does South Africa's NTP Radioisotopes. Although the entry of these companies in the U.S. market has made U.S. users somewhat less vulnerable to problems at NRU, the November–December 2007 shutdown, cited above, is emblematic of the fact that supplies still remain insufficiently flexible. While mostly an inconvenience, the situation was "potentially dangerous for a small number of patients with certain conditions," according to J. James Frost, a Yale University professor of diagnostic radiology.[37]

Reducing the Risk of Using HEU in the Civilian Nuclear Sector

Although no serious terrorist attempts to construct an IND have ever been uncovered, terrorism experts cite increasing indications of dangerous groups desiring to create and use an IND.[38] Even without state assistance, U.S. nuclear weapons experts agree that some terrorist groups would be technically capable of constructing a primitive nuclear device, if they were able to obtain the necessary fissile materials. Department of Homeland Security (DHS) reports note that its experts do not believe that terrorists can enrich uranium or breed plutonium. Therefore, DHS avers that the only way a terrorist could access such materials is by theft from a fuel cycle facility, purchase on the black market, or transfer from a state sponsor.[39] Since HEU can be used in the construction of a gun-type nuclear device (the crudest type of nuclear bomb and the one most within the capabilities of non-state actors), ensuring that such actors do not have access to HEU is critical.

The risks of isotope production have not gone unnoticed by policy makers. While the RERTR program initially focused on nuclear fuel, it has also researched methods to eliminate the use of HEU targets in Mo-99 production since the mid-1980s. However, RERTR had few means to persuade foreign reactor operators or producers of Mo-99 to cooperate with it until the October 1992 passage of the Schumer Amendment (henceforth referred to as Schumer, after then-Representative Charles Schumer, Democrat of New York) to the Energy Policy Act.[40] Schumer limited U.S. exports of HEU to facilities that met several conditions. First, the facility had to lack an existing alternative LEU production process. Second, the facility had to agree to switch to LEU when possible. And third, the United States had to be actively developing an alternative LEU production process suitable for the facility.[41] As a result, according to data from the U.S. Nuclear Regulatory Commission (NRC), exports of HEU for medical isotope production fell to just a handful by 2005.[42] While the major reduction in HEU exports came from reduced shipments of nuclear fuel, the impact on Mo-99 production was also important.

Before Schumer, RERTR had managed to persuade Argentina to work on conversion of its Mo-99 process. But RERTR had been unable either to get Canadian buy-in, or to secure sufficient funding for work on developing the technologies needed for conversion (all RERTR work on conversion of isotope production stopped from fiscal 1990 to late fiscal 1993 due to a lack of money).[43] Along with the adoption of the Schumer Amendment, Congress also began to give RERTR efforts greater financial support, increasing funding dramatically in 1994, including about $1 million annually for isotope conversion, allowing "a multi-front R&D program and significant cooperation with multiple producers."[44] While cooperation with smaller producers in Argentina, Australia, and Indonesia had proved very fruitful, Argonne National Laboratory scientists working on isotope conversion under RERTR later reported that interactions with major producers continued to face ups and downs. For example, in January 2001, Nordion provided a plan of work that would need to be accomplished in order for conversion to occur. It identified three phases (estimating at the time that the entire program would take less than a decade): (1) an initial feasibility study, which had already been completed; (2) a conversion development program, scheduled for completion in 2003; and (3) a conversion implementation program that would take an additional three years.[45] Unfortunately, cooperation with MDS Nordion noticeably declined at the end of 2002 and ceased altogether following the passage of the Energy Policy Act of 2005, discussed below.[46]

U.S. pressure has been critical for RERTR progress in the past. Further steps toward HEU elimination are similarly unlikely without Schumer-like legislation. Nordion and AECL, which operates the Canadian reactors, promised early on to develop an LEU target by 1998 and to "phase out HEU use by 2000."[47] Turning these promises into action, though, often required the direct incentive of an application for HEU imports. It was when it sought a U.S. export license for HEU in 1999 that Nordion pledged to submit annual progress reports on its conversion efforts. Similarly, the company had a pattern of providing information to RERTR scientists when seeking such export licenses. However, when pressure was off, the company seemed less forthcoming, citing commercial secrecy issues (according to scientists at Argonne National Laboratory, who indicate that Nordion's information remains more sparse than data received from European producers).

In the last decade, Nordion did not act to make conversion to LEU easy. It built a new isotope processing facility, the NPF, which was optimized for HEU targets. Although initially stating that the new facility could be modified to handle LEU targets, in 2003 Nordion conceded that conversion was not feasible without a significant interruption in production. Instead, yet another processing facility would have to be built for the LEU line, entailing unacceptable costs ($90 million Canadian). According to Alan Kuperman—a senior policy analyst at the nongovernmental Nuclear Control Institute and a strong advocate on HEU issues in Congress for a decade and a half—instead of actively cooperating with the RERTR program, Nordion chose to lobby for amending the law and reducing the restrictions on U.S. transfers of HEU.[48]

If the Schumer Amendment had stayed in force, the U.S. government would likely have moved forward with plans to encourage governments worldwide to adopt HEU guidelines (discussed in the concluding article of this special section), as well as with diplomatic initiatives to gain an agreement among major isotope producers to coordinate conversion plans and thereby remove competitive concerns. The possibility that a producer might take advantage of the conversion process to make competitive gains has been one of the factors causing major producers to shy away from conversion commitments. To address this problem, in 1999 the Nuclear Control Institute proposed that all producers pledge to convert as quickly as possible and cooperate in developing conversion technologies, to avoid competitive disadvantages.[49] The RERTR program put forward its own proposed language, and producers signaled their willingness to discuss such a pledge. However, soon thereafter the U.S. State Department decided that governments might object to an attempt to come to an agreement with producers in their countries, viewing it as "meddling" in their domestic affairs, and, therefore, decided to call a meeting of their governmental counterparts to discuss the development of a common policy. But a meeting scheduled for late 2005 was canceled after the adoption of the so-called Burr Amendment to the Energy Policy Act (after Representative Richard M. Burr, Republican of North Carolina). No further attempts have been made to come to an agreement since that time. However, representatives of major isotope production companies continue to voice their concern on issues of competitiveness. While they would like assurances that conversion will not detrimentally affect their market positions, some new producers have argued that there should be nothing sacred about the commercial position of major producers. Indeed, there is logic to U.S. consumers helping U.S. and not foreign producers, and in providing preferences to LEU-based production. There has yet to be any attempt to legislate any sort of preferences—tax breaks, direct financial assistance, or any other sort of advantages—for LEU users.

U.S. law has actually changed to the detriment of LEU conversion. Several years of Nordion lobbying culminated in the July 2005 adoption of the Burr Amendment, which relaxed the Schumer provisions that had been critical to gaining the cooperation of foreign facilities with RERTR. In particular, under Burr, U.S. HEU may now be exported to medical isotope producers in Europe and Canada (though not elsewhere) without the condition of agreeing to convert to LEU.[50] More positively, the 2005 Energy Act did include language requiring the DOE to contract with the National Academy of Sciences (NAS) for a study into the feasibility of producing Mo-99 using LEU. The law defined production to be feasible if: LEU targets have been developed and demonstrated for use in the reactors and target processing facilities that produce significant quantities of medical isotopes to serve U.S. needs for such isotopes; sufficient quantities of medical isotopes are available from LEU targets and fuel to meet U.S. domestic needs; and the average anticipated total cost increase from production of medical isotopes in such facilities without use of HEU is less than 10 percent.[51]

There have since been arguments as to whether this 10 percent cost increase is to the producer or consumer. Princeton University's Frank von Hippel has pointed out that converting to LEU would have a negligible effect on the cost of medical isotopes for patients, the price that ought to be of chief concern to Congress.[52] NAS study participants have reportedly decided that their report will contain estimates of cost implications for both the isotope producers and consumers. Furthermore, the Energy Act states that if the NAS study determines supply of Mo-99 using LEU is feasible but cannot report that major producers have made the commitment to convert to such production, then DOE should submit no later than in 2011 a report on the options for developing domestic supplies without the use of HEU to Congress.[53]

The world's other three major suppliers, though wary of conversion costs, have not lobbied as heavily against it. The Nuclear Energy Corporation of South Africa (NECSA), parent company of NTP Radioisotopes, which currently supplies some 15 percent of the world's Mo-99 (and is the only producer with a fully independent source of enriched uranium), recently suggested that it has been looking at LEU-based technologies, viewing them as a possible competitive edge if countries were to adopt policies favoring imports of LEU-based Mo-99 production.[54] NECSA is looking to use a type of target that could already be produced by the French nuclear fuel manufacturer CERCA with current equipment.[55]

At a recent meeting on converting Mo-99 production to LEU held in Sydney, Australia, the manager of the High Flux Reactor (HFR) at Petten, in the Netherlands, which irradiates targets for IRE and Covidien, stated that the Nuclear Research & consultancy Group (NRG)—operator of the HFR—would begin work to develop LEU targets in cooperation with France's CERCA. Such targets might be used in the HFR, while the new Pallas reactor, scheduled to replace HFR in 2015, will be designed to use LEU fuel and targets from the outset.[56] The forthcoming feasibility study could lead to qualification irradiation of "monolithic" LEU targets within a few years and large-scale production of Mo-99 from LEU within a decade, according to NRG.[57] A spokesman for CERCA, the French nuclear company, said at the Sydney meeting that a survey of future needs suggests there will be a demand for some 5,000–10,000 LEU targets per year, and that CERCA has decided to invest in development of LEU targets. However, production of targets for NRG would involve new equipment, since the HFR reactor would use a monolithic LEU target, rather than the "dispersion" target used by NECSA. While CERCA believes it can create an industrial production capacity to produce these targets in three to four years, it needs partner companies or governments to help fund this investment. CERCA has been in talks with Petten and the Missouri University Research Reactor (MURR) on developing LEU targets. However, full-scale industrial production is not likely to be set up without either a government mandate or government funding.[58]

Expanding LEU-Based Production, Encouraging Conversion

Lobbyists who promoted the 2005 changes to U.S. legislation claimed that conversion to LEU would be too costly and could disrupt production of medical isotopes. While the up-front costs of conversion to LEU are considerable, there is increasing evidence that operational costs after conversion will not be significantly higher than using HEU. Furthermore, new LEU-based production—as compared to converting existing production—could well obviate the argument that medical isotope production could be disrupted by conversion requirements—an argument that was particularly important to some policy makers and garnered support from the medical establishment. If new LEU-based Mo-99 production takes off in the next few years, the pressure to continue sales of HEU to today's major producers will be reduced.

In fact, there is already a small but growing amount of Mo-99 production derived from the irradiation of LEU targets.[59] Argentina began commercial production of Mo-99 using LEU targets in 2002; Australia will soon begin large-scale LEU-based production; the IAEA is assisting a number of countries in examining and testing the use of LEU targets; and several U.S. reactors are launching pilot projects using LEU targets that could lead to major production of Mo-99 (possibly meeting the needs of the entire U.S. market in a decade's time).[60] In addition to the production of Mo-99 by fission of U-235 and irradiation of uranium targets (the most prevalent process), Mo-99 can also be produced by means of neutron activation.[61] China, India, Brazil, Kazakhstan, and Iran all have neutron activation programs and supply local users. In still another method, which is only in the research stage, Mo-99 is produced using an aqueous homogenous reactor (also referred to as a "solution" reactor, discussed below). The creation of significant new LEU-based Mo-99 production capacities might well reduce incentives for U.S. policy makers to continue support of the Burr Amendment. Without such a change in U.S. HEU export policy, or the investment by the United States and/or other governments in the conversion of major Mo-99 producers, however, it seems unlikely that major producers will wish to undertake the up-front costs of converting to LEU targets.

Converting existing Mo-99 production from HEU to LEU targets involves substantial up-front costs because both the design and chemical processing of the target is different when LEU is used. Nevertheless, some worries about long-term costs do not withstand close scrutiny. For example, some observers have worried about increased wastes with the use of LEU targets. However, though there is five times more uranium in the LEU targets, which means five times more uranium in liquid target waste, the total volume of waste from LEU is not greater, and may even be slightly less, than in the current HEU process.[62] Argonne's George Vandegrift has said that after conversion, waste costs would likely be less than before conversion. Furthermore, Mo-99 production using LEU targets has been demonstrated to not affect product purity, product yield, or operating costs. Up-front conversion costs, however, are significant. Further, as noted by Vandegrift, "large-scale technology for conversion to LEU targets can never be completely demonstrated without the cooperation of the commercial producers." This makes it particularly important to obtain the cooperation of the major producers with the RERTR program. Their cooperation in an IAEA Coordinated Research Project (CRP) on Mo-99 production using LEU is therefore most welcome. However, in-depth cooperation with RERTR scientists at Argonne, particularly on the part of Nordion, needs to improve if conversion efforts are to advance.

Several organizations have worked on the development of technologies to produce Mo-99 in homogenous aqueous liquid nuclear reactors (also known as solution reactors), without the use of targets.[63] In 1992, Russell Ball, then of BWX Technologies (now part of Babcock and Wilcox, B&W), patented a process of "targetless" Mo-99 production using an aqueous homogenous reactor fueled with uranyl nitrate (which, it was anticipated, could use LEU fuel).[64] The advantages of this system include: low cost, targets are unnecessary, there is far less waste (one one-hundredth of the total produced in the target method for a given quantity of Mo-99), the extraction processing is simplified (since no uranium dissolution is required), and inherent passive safety.[65] In 1998, Ball, then with Technology Commercialization International (known as TCI Medical), cooperated with Vladimir Pavshuk and Vladimir Khvostionov of Russia's Kurchatov Institute on further research to commercialize the method. They successfully produced Mo-99 in Kurchatov's HEU-fueled ARGUS reactor that, after purification, met U.S. Pharmacopoeia (FDA) requirements.[66] Although pharmaceutical companies tend to have still higher purity requirements, the chemical processes that would have to be used to reach the needed purity level are well known.[67] TCI Medical continued to cooperate with Kurchatov for several years, developing a Mo-99 machine based on a uranyl sulphate solution that they believed is commercially promising.[68] Unfortunately, however, TCI ran into financial problems unrelated to its Mo-99 project and ceased operations. B&W remains interested in the use of a uranyl nitrate solution machine to produce Mo-99 and is continuing feasibility studies in this area, this time fueling the reactor with LEU. But the company has yet to attract significant financing to pursue either the development of hardware or of production protocols, which are necessary to meet FDA standards. Although technetium is only 10 percent of the cost of radiopharmaceuticals, it is fairly expensive to produce; distribution is also complex and difficult to set up. While there is insufficient back-up supply today, the major producers are able to meet current demand under normal circumstances (when there are no reactor, processing, or distribution problems). This is why it has been quite difficult to attract investment in new production. Although the U.S. government is interested in nonproliferation, DOE can only fund research related to new technologies, not invest in new production.[69]

B&W is currently seeking a pharmaceutical company to partner with in the effort to bring the solution reactor method of Mo-99 production to market.[70] Given funds, B&W experts estimate that an operation could be up and running in five to six years.[71] In June 2007, the IAEA held a consultancy meeting on homogenous reactors dedicated to radioisotope production.[72] Meeting participants highlighted the many possible benefits of solution reactors but noted that significant challenges to commercial production remain, including development of isotope separation technology, increasing reactor power beyond operating experience, and licensing production of medical isotopes in such a system (relevant regulations do not currently exist).[73] Consultancy recommendations included the initiation of an IAEA CRP on solution reactors and medical isotope processing; the agency is currently seeking funding for this activity.[74]

Another possible way to produce Mo-99 is with an accelerator-driven subcritical assembly. Joint research on this method has been undertaken by the Kharkiv Institute of Physics and Technology, in Ukraine, as well as by the Belgian Nuclear Research Center.[75] Resulting Mo-99 would reportedly be of standard (good) quality, though the system is as yet unproven.

As noted above, there is also a small yet growing volume of Mo-99 being made from the irradiation of molybdenum-98 (using gel generators and neutron activation) to produce Tc-99m, principally in Brazil, China, and India. India, for example, has commissioned a production facility for gel generators, supplying them to hospital radiopharmacies.[76]

In late 2004, a meeting on gel generators led to an IAEA CRP to help countries begin small-scale production of Mo-99 using LEU targets or gel generators.[77] Since that time, research contracts and agreements have been concluded with institutions in Argentina, Chile, India, Indonesia, Kazakhstan, Libya, Pakistan, Poland, Romania, South Korea, and the United States to conduct research on production of Mo-99 using an LEU-modified Cintichem process and using gel generators.

Despite the progress cited above, major radioisotope producers continue to have questions regarding the feasibility of shifting to LEU targets, even though experts at DOE and elsewhere affirm that there are no technical issues to prevent conversion. Indeed, the Argentine Mo-99 producer has observed an improvement of radionuclide purity and yield since changing to LEU.[78] What is more, with conversion, other useful isotopes such as iodine 131 (I-131) can be recovered, instead of leaving them as waste in the Mo-99 production process.[79] (Argentina began I-131 production in September 2005, for instance.) However, all current LEU fission production is small-scale; Australia's ANSTO, the first producer with large-scale plans, will only begin to scale up in the next year. Meanwhile, major producers raise questions about whether problems will arise as a process is scaled up. For example, higher levels of radiation due to larger-scale processing could reduce molybdenum yield.[80]

Conversion can already be deemed a success, though, in countries with less demand. The National Atomic Energy Commission of Argentina (CNEA) was the first institute in the world to convert from fission production of Mo-99 with HEU to LEU.[81] CNEA began production of Mo-99 with HEU in 1985; LEU-silicide target development in 1990–1994; development of LEU metal foil targets in 1999 (with U.S. cooperation); LEU aluminide target development in 2001; and finally production of fission Mo-99 with LEU in 2002.[82] Argentina subsequently sold its LEU target technology to Australia and Egypt. This has provided substantial economic benefits, though the decision to turn to the use of LEU targets was only reached in 2001 "due to the final [Schumer Amendment] restriction on the supply of HEU material for the production of fission Mo-99."[83] It should be noted that small producers would like to expand their market share and do not view the Burr Amendment as helpful—or fair. At the RERTR 2006 International Meeting, CNEA's Horacio Taboada said that in allowing just five providers to receive HEU from the United States, the new U.S. legislation employed a "double standard" that contradicts HEU minimization policy.[84]

One recent development that could persuade U.S. legislators to alter this legislation yet again is the prospect of no longer having to rely on Nordion for radioisotopes. Several U.S. institutions are seriously pursuing the establishment of LEU-based Mo-99 production. The University of Missouri's MURR research reactor (located in Columbia, Missouri), for example, is involved in a serious effort to produce Mo-99. As of March 2008, MURR was awaiting NRC approval for demonstration irradiation and processing of LEU targets, expected in late spring 2008.[85] MURR intends to make a final decision on target design by fall 2008 and apply for a production facility license in spring 2009. If all goes as planned, construction would begin in late 2009, with commercial operation expected by 2012.[86] MURR's long-term objective, if the trial indicates that it is feasible, is to supply 30–50 percent of current U.S. demand for Mo-99.[87] This is a critical project for ensuring reliability of supply in the U.S. market; relying on a foreign source of supply is increasingly risky in this age of terrorism, when the U.S. or other borders might be suddenly closed.[88] Although MURR will have difficulty meeting its goals—particularly its ambitious timeline—without government financial and regulatory support, the U.S. government restricts the assistance it provides for the project so as not to give MURR an unfair competitive advantage. Given the Canadian funding that AECL has received for reactor construction, and the fact that there are no current U.S. competitors, this decision does not seem to be in the interest of either the U.S. taxpayer or U.S. industry.

Conclusion

Production of Mo-99 will soon consume half of the HEU employed in the civilian sphere. The HEU targets used to produce Mo-99 are only lightly irradiated, posing risks that are greater than spent fuel rods at research reactors. In addition, Mo-99 producers have large quantities of HEU target waste on-site, while many reactor facilities have far smaller amounts of spent fuel. Though it is not extremely likely that a terrorist will steal material in Chalk River, Canada, and create a nuclear device that is detonated in a North American city, it is not impossible. If nuclear terrorism is to be prevented, then Mo-99 production should be recognized as an increasingly weak link.

The LEU technology compatible with large-scale Mo-99 production, including target technology and dissolution and waste management processes, is largely understood. However, engineering a large-scale commercial solution will require both time and money. Full cooperation of producers and sufficient funding from interested parties are needed to make total conversion in the next decade possible. If policy makers do not insist that producers share their processes with RERTR, then the program will not be able to assist in developing a conversion process, and producers will have to formulate such processes for themselves. Although some companies have taken initial steps in this direction, they may not be willing or able to foot the entire bill. Governments must decide if they will provide financial assistance, insist upon conversion through disincentives (such as Schumer-like legislation or perhaps taxation or other financial penalties), or simply maintain the status quo. The current situation poses grave risks. This is an issue with financial, political, and security implications and should be discussed and decided on its merits: the global community should not continue to operate on autopilot, without consideration given to the real risks and costs, along with possible solutions.

Commercial producers will likely fund conversion if they believe consumers or world policy makers insist on it. The recent moves by NECSA, Petten, and CERCA, like ANSTO, Missouri University, CNEA, and BATAN Indonesia before them, show that there has been movement in this direction. Costs may well be passed on to consumers (over time, a marginal cost increase likely to be so small as to be almost unnoticeable to the consumer). Of course, in the short run, costs appear quite large to producers. Thus, national governments may do well to consider provisions of financial assistance to aid this project. International bodies should give nonproliferation credit for monies spent on such an effort (for example, letting such funding count toward pledges under the Group of Eight Global Partnership program).

Another major obstacle to conversion is the difficulty in ensuring that Mo-99 supplies continue uninterrupted as conversion moves forward. This process requires various problems to be solved, including how to ensure sufficiently rapid licensing of new facilities and new pharmaceuticals, and how to deal with the possible impact of the downtime of individual facilities on patients and on competitiveness. Government commitment and assistance is needed to make certain that new production, critical to ensure future supplies—even were conversion efforts to cease—comes online in a timely fashion. Particular support should be given to new facilities—whether existing reactors that have yet to begin commercial Mo-99 production, or completely new facilities in new countries, such as the United States or Egypt—to ensure regional availability of Mo-99. It is clear that existing producers might not want new competition, but they themselves have pointed out the need for increased global production capacity.

The commitment of the U.S. government is particularly critical where Mo-99 conversion is concerned. Not only is the United States the biggest single market for medical isotopes, it is also the major exporter of HEU for the fabrication of targets for Mo-99 production, and should be able to use this leverage to get cooperation with its conversion goals. The Schumer Amendment was very successful in this regard. Since it was overturned in 2005, the DOE has had little leverage to engage producers. Nordion, in particular, has often claimed production processes to be commercial secrets, even though

DOE personnel have had access to similar information for European facilities. Without this information, the RERTR program will be unable to determine how to reengineer the Nordion process for the use of LEU.

It is difficult to understand why there has been so little Canadian government engagement on this issue, though the November–December 2007 reactor problems in Canada could possibly change this situation. To date, Canadian diplomats have instead pointed out that they have never been suspected of diverting nuclear materials for weapons use, nor have there been any known thefts of nuclear material from their facilities. They evidently do not view HEU as posing risks (though there is no evidence of a recent evaluation of the risks posed), at least domestically. Thus, the only incentive for cooperation with the RERTR program is if it is mandated for the import of U.S. HEU. A decade ago Canadian stakeholders argued that it would take them six to eight years to convert. Today Nordion says it would take up to a decade. While conversion cannot happen overnight, one might wonder how many more decades will pass before initiating the countdown to conversion.

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NOTES

1. AECL, operator of the NRU reactor, had reportedly provided Canada's Nuclear Safety Commission written confirmation that all required safety system upgrades were installed by December 31, 2005, and received a renewed license to operate the reactor on that basis. However, two mandated heavy water pumps were not connected to an emergency power supply. The discovery of this fact in November 2007 led to the extension of a routine NRU shutdown affecting Tc-99m sold both by Nordion and by Covidien throughout North America. South Africa provided some back-up supply, but European producers were unable to respond for more than two weeks. By that time, Canadian parliament had passed an emergency measure to order the restart of the reactor and connection of the emergency power supplies. The reactor was restarted on December 16, and production of radioisotopes resumed on December 18. "Backgrounder: Safety Upgrades: Atomic Energy of Canada Limited's National Research Universal Nuclear Reactor," Canadian Nuclear Safety Commission (CNSC), December 10, 2007, <www.nuclearsafety.gc.ca/eng/newsroom/issues/backg_precis_aecl_iso.cfm>; "CNSC and AECL to Conduct Joint Review of NRU Reactor Events," February 14, 2008, AECL, <www.aecl.ca/NewsRoom/News/Press-2008/080214.htm>; "MDS Nordion Responds to 'Canada's Nuclear Fallout' Article," *CMAJ*, February 6, 2008, <www.cmaj.ca/cgi/eletters/cmaj.080154v1>.
2. Shawn McCarthy, "Ottawa Got Early Warning, Firm Says," *Globe and Mail,* February 8, 2008.
3. Werner Swart and Melody Brandon, "Nuclear Alert," *The Times* (South Africa), November 14, 2007; Michael Wines, "Break-In at Nuclear Site Baffles South Africa," *New York Times*, November 15, 2007, p. A3.

4. Another breach approximately two years ago reportedly led to a security upgrade. Micah Zenko, ''A Nuclear Site Is Breached: South African Attack Should Sound Alarms,'' December 20, 2007, *Washington Post*, p. A29.
5. ''Workshop Report,'' Global Initiative to Combat Nuclear Terrorism: Workshop on the Production of Mo-99 Using Low Enriched Uranium, December 2–5, 2007, Sydney, Australia.
6. George Vandegrift, ''Primer on Mo-99 Production,'' white paper written for the NAS study on the production of medical isotopes without HEU, mandated by Section 630 of the Energy Policy Act of 2005.
7. The Tc-99m can be eluted (milked) from the Mo-99 generator once a day (Mo-99 is retained). The generators lose half their activity every sixty-six hours (the half-life of Mo-99) and are generally replaced once a week. Generators contain 0.5 to 10 curies of Mo-99. Vandegrift, ''Primer on Mo-99 Production.''
8. About half of the Mo-99 used in the world is used in nuclear medicine in the United States. Forecasts by producers predict some 5–10 percent growth in U.S. annual demand for Mo-99 over the next decade and 8–12 percent growth in world demand.
9. The world's four major producers use HEU targets, while much of the remaining 5 percent of global Mo-99 production is derived from the irradiation of LEU targets. The targets are essentially mini-HEU fuel plates, where a uranium-aluminum alloy or compound is mixed with aluminum powder and sandwiched between two pieces of aluminum cladding, either flat or cylindrical in form. The number of days of irradiation depends upon the flux of the reactor and other factors, but is generally less than a week. The targets are thus nowhere near as radioactive as spent fuel elements after irradiation. Vandegrift, ''Primer on Mo-99 Production.''
10. Producers generally sell Mo-99 by the ''six-day curie.'' This means they assure that, six days after delivery, the number of curies will decay to no more than the specified amount. Given the sixty-six hour half-life, the producers must actually send about four times the number of curies that will be available six days later. Ibid.
11. For more information on the RERTR program, see the article by William C. Potter and the article by Anya Loukianova and Cristina Hansell in the special section in this issue. For statistics comparing the use of HEU in research reactor fuel and the production of Mo-99, see discussion below as well as the article by Ole Reistad and Styrkaar Hustveit in the special section in this issue.
12. A presentation by experts from Belgium's Institut National des Radioéléments and Nuclear Research Center stated that there would be a ''definitive need'' for one new reactor in Europe by 2010–2015 for radioisotope production, and a possible need for a second new reactor for this purpose by 2015–2020. Henri Bonet, Bernard David, and Bernard Ponsard, ''Production of Mo99 in Europe: Status and Perspectives,'' Research Reactor Fuel Management Meeting, Budapest, Hungary, April 2005.
13. PUREX stands for plutonium-uranium extraction. See George Vandegrift, Allen J. Bakel, and Justin W. Thomas, ''Overview of 2007 ANL Progress for Conversion of HEU Based Mo-99 Production as Part of the U.S. Global Threat Reduction—Conversion Program,'' paper presented at the RERTR 2007 International Meeting, Prague, September 23–27, 2007. According to the calculations in this study, the dose rate per gram of HEU irradiated for five days at a flux of $1x10^{14}$ neutrons per square centimeter (cm) per second drops by nearly five orders of magnitude from the day the target is processed until the end of three years in storage. Calculating dose rates after three years for the two types of processing methods used by major producers, it was determined that for acid-dissolution waste, the dose rate after three years of storage is 1.5 mrem per hour per gram of HEU at 100 cm, with no shielding. For alkaline-digested HEU, the dose rate is 0.5 mrem. Any shielding would considerably lower this dose rate.
14. Ibid.
15. The study by Vandegrift, Bakel, and Thomas uses the spent research reactor fuel dose rate cited in: Raymond B. Pond and James E. Matos, ''Nuclear Mass Inventory, Photon Dose Rate, and Thermal Decay Heat of Spent Research Reactor Fuel Assemblies (Rev 1),'' paper presented at the RERTR 1996 International Meeting, Seoul, October 6–10, 1996. See also Vandegrift, Bakel, and Thomas, ''Overview of 2007 ANL Progress.''
16. Such as RERTR, the U.S. Foreign Research Reactor Spent Nuclear Fuel (FRR SNF) acceptance program, the Russian Research Reactor Fuel Return (RRRFR) program, the Emerging Threats and Gap Material Program, and the Global Research Reactor Security (GRRS) Program. For more information, see the article by Anya Loukianova and Cristina Hansell in the special section in this issue.

17. For a description of security of U.S. HEU and new U.S. requirements, see the article by Anya Loukianova and Cristina Hansell in the special section in this issue.

18. IAEA, ''The Physical Protection of Nuclear Material and Nuclear Facilities,'' INFCIRC/225/Rev.4.

19. ''The Technetium-99m Generator,'' Brookhaven National Laboratory, <www.bnl.gov/bnlweb/history/Tc-99m.asp>.

20. Ibid.

21. ''Canada's Nuclear History Chronology,'' Canadian Nuclear Society, updated March 13, 2008, <www.cns-snc.ca/history/canadian_nuclear_history.html>.

22. ''Record of Decision for the Medical Isotopes Production Project: Molybdenum-99 and Related Isotopes,'' *Federal Register*, Vol. 61, No. 181 (September 17, 1996), pp. 48921–48928.

23. S. James Adelstein and Frederick J. Manning, eds., *Isotopes for Medicine and the Life Sciences* (Washington, DC: National Academies Press, 1995).

24. Kathryn Ostic, ''Laboratory Decommissioning Omega West Reactor Starting Next Month,'' *Los Alamos National Laboratory News Bulletin*, May 15, 2002.

25. The Energy and Water Development Appropriations Act of 1990 required isotope production and distribution to be self-supporting as of fiscal 1990. Adelstein and Manning, *Isotopes for Medicine and the Life Sciences*.

26. J. Rojas-Burke, ''The Future Supply of Molybdenum-99,'' *Journal of Nuclear Medicine* 36 (November 1995), pp. 15N, 22N, 35N; Darren G. Talley, ''Isotope Production Target Irradiation Experience at the Annular Core Research Reactor,'' DOE document, SAND97-0308C (1997); ''Record of Decision for the Medical Isotopes Production Project: Molybdenum-99 and Related Isotopes.''

27. Letter from Tom Clements, Nuclear Control Institute, to Colette E. Brown, Office of Nuclear Energy, Science and Technology, DOE , September 18, 2000, <www.nci.org/f/fftf91800.htm>.

28. Adelstein and Manning, *Isotopes for Medicine and the Life Sciences*.

29. ''Record of Decision for the Medical Isotopes Production Project: Molybdenum-99 and Related Isotopes.''

30. Ibid.

31. See December 13, 2007 letter from Rick Lytle, U.S. general manager, Imaging Solutions, Covidien, to Covidien customers regarding the December 2007 shortage, <www.imaging.mallinckrodt.com/_Attachments/Resources/Covidien%20Mo99%20CUSTOMER%20Update%2012-13-07%20Final.pdf>.

32. ''Sudden Radioisotope Shortage Threatens Patient Care,'' *Journal of Nuclear Medicine* 49 (January 2008), pp. 17N–18N.

33. McCarthy, ''Ottawa Got Early Warning, Firm Says.''

34. Alan Kuperman notes that European and South African reactors typically operate well below capacity, arguing that back-up supplies could have been made available. He has called for a thorough investigation into the November 2007 events. See Alan Kuperman, ''Backup Supplies Were Readily Available from Reactors in Europe and South Africa,'' *Toronto Star*, March 1, 2008.

35. Alexandre Deslongchamps, ''Atomic Energy Scraps Plans for Isotope Reactors (Update 2),'' Bloomberg News, May 16, 2008.

36. ''Mallinckrodt Product Clearances Total Nearly 40 Worldwide During 1997,'' PR Newswire, February 23, 1998; ''Future of Nuclear Medicine, Part 1: Marketing Research Forecasts,'' *Journal of Nuclear Medicine* 39 (February 1998), pp. 27N–28N, 30N.

37. Ian Austen, ''Reactor Shutdown Causing Medical Isotope Shortage,'' *New York Times*, December 6, 2007, p. C5.

38. For a brief history of terrorist attacks and insightful assessment of terrorist trends, predicting that terrorist groups are more likely to seek weapons of mass destruction in the future than they were in the past, see Richard Falkenrath, ''Confronting Nuclear, Biological, and Chemical Terrorism,'' *Survival* 40 (Autumn 1998), pp. 42–65.

39. ''Nuclear Smuggling,'' undated, Department of Homeland Security Nuclear Assessment Program, <www.exportcontrol.org/library/conferences/1379/005_Proliferation_Threat_Brief-Nuclear_Smuggling_-_Zachary_K.pdf>.

40. For more information on the Schumer Amendment, see the article by Anya Loukianova and Cristina Hansell in the special section in this issue.

41. U.S. Public Law 102–486 (106 Stat. 2943), October 24, 1992.

42. NRC officials, e-mail correspondence with Scott Parrish, Center for Nonproliferation Studies, May 2005. (Interviews granted on condition of anonymity.)
43. George F. Vandegrift, ''RERTR/GTRI Mo-99 Technology-Development History,'' Argonne National Laboratory, unpublished paper, April 2007.
44. Vandegrift, ''RERTR/GTRI Mo-99 Technology-Development History.''
45. George Vandegrift, ''ANL (GFV) Perspective on Conversion of Mo-99 Production from High- to Low-Enriched Uranium,'' presentation for the NAS study on the production of medical isotopes without HEU, mandated by Section 630 of the Energy Policy Act of 2005, Argonne National Laboratory, <dels.nas.edu/nrsb/presentations/vandergrift.pdf>.
46. Ibid.
47. Alan J. Kuperman, ''The Global Threat Reduction Initiative and Conversion of Isotope Production to LEU Targets,'' paper presented at the RERTR 2004 International Meeting, Vienna, November 7–11, 2004, p. 3.
48. For details about Nordion lobbying and the Burr Amendment, see Alan Kuperman, ''Bomb-Grade Bazaar,'' *Bulletin of the Atomic Scientists,* March/April 2006, pp. 44–50.
49. Kuperman, ''The Global Threat Reduction Initiative and Conversion of Isotope Production to LEU Targets.''
50. The bill passed the House on July 27, 2005 by 275–156 and the Senate on July 29, 2005 by 74–26. H.R. 6, Energy Policy Act of 2005. It is now known as Public Law 109-58.
51. Energy Policy Act of 2005 (P.L. 109-58).
52. Frank N. von Hippel and Laura H. Kahn, ''Feasibility of Eliminating the Use of Highly Enriched Uranium in the Production of Medical Radioisotopes,'' *Science and Global Security* 14 (2006), p. 157.
53. Energy Policy Act of 2005 (P.L. 109-58).
54. NESCA, *NECSA Annual Report 2006*, p. 35, <www.necsa.co.za/docs/K-4685_NECSA_Annual Report_2006_LR.pdf>; Nicky Smith, ''Second Reactor Mooted,'' *Financial Mail*, November 23, 2007, p. 76.
55. CERCA produces aluminide (UAlx) and silicide (U3Si2) ''dispersion'' research reactor fuel on the same type of equipment needed to produce dispersed uranium targets. It has already demonstrated laboratory-scale production of these targets, has a partnership with NECSA, and is in talks with Australia's ANSTO. Presentation by Jean Louis Falgoux, Areva vice president, at the Global Initiative to Combat Nuclear Terrorism Workshop on Molybdenum-99 Production Using Low Enriched Uranium, Sydney, Australia, December 2–5, 2007.
56. HFR's share of the global Mo-99 market was about 30 percent and its European market share 60 percent as of 2006. European Commission, ''A Joint Undertaking Initiative for the High Flux Reactor,'' 2006.
57. Ann MacLachlan, ''NRG to Study Potential for use of LEU for Mo-99,'' *Nuclear Fuel*, December 17, 2007, p. 1.
58. Isotope producer IRE, which receives some of its irradiation services at HFR, was apparently unaware of the NRG plan before the Sydney meeting. IRE director Henri Bonet expressed some doubt about the time frame suggested by the HFR director, noting that world Mo-99 demand is increasing and must be met at the same time. Further, he estimated that the new processing facilities that would have to be built to handle LEU targets would cost 50 million–100 million euros. Nevertheless, representatives of all of the major isotope producers agreed at the Sydney workshop that industrial-scale production using LEU targets could be introduced in seven to ten years. Ann MacLachlan, ''NRG to Study Potential for Use of LEU for Mo-99.''
59. IAEA, ''CRP on Production of Mo-99 from LEU or Neutron Activation,'' <www.iaea.org/OurWork/ST/NE/NEFW/nfcms_researchreactors_Mo99.html>.
60. ANSTO plans to increase production from 500,000 doses per year to some 2 million doses per year (just under 10 percent of current world demand). Indonesia is converting to LEU targets in 2008; conversion has been slowed by difficulties obtaining U.S. export licenses for its new LEU targets. Budi Briyatmoko, Sudarmadi Abdul Mutalib, and Bambang Purwadi, ''Indonesia's Program for Conversion of Mo-99 Production to LEU Fission,'' presentation at the Symposium on Minimization of HEU in the Civilian Nuclear Sector,'' Oslo, Norway, June 17–20, 2006; DOE scientist (name withheld at author's discretion), statement at Global Initiative to Combat Nuclear Terrorism: Workshop on the Production of Mo-99 Using Low Enriched Uranium, December 2–5, 2007, Sydney, Australia.

61. MURR produced Mo-99 from neutron activation for domestic use beginning in 1967. It ceased in 1984 when Mo-99 from fission became readily available and the smaller market for neutron activation disappeared. Ralph Butler, director, Research Reactor Center, University of Missouri-Columbia, personal correspondence with author, March 24, 2008.
62. Argonne's George Vandegrift notes that "use of the LEU-foil target in alkaline-digestion processes will reduce liquid waste volumes by at least five times and greatly limit the amount of aluminum hydroxide and column material that must be disposed. In the Cintichem process, lower dissolution volume may generate slightly less waste." George F. Vandegrift, "Facts and Myths Concerning 99Mo Production with HEU and LEU Targets," paper presented at the RERTR 2005 International Meeting, Boston, November 6–10, 2005.
63. More than thirty such reactors have been built. Currently, there are homogenous reactors: at Los Alamos (seven reactors) and Oak Ridge (two) in the United States; at IPPE Obninsk (two) and Kurchatov (two) in Russia; at Valduc, France (two critical assemblies); and at JAERI and Tokai (two critical assemblies) in Japan. Alberto Manzini, "Producing Mo-99 from LEU Targets," presentation at the Symposium on Minimization of HEU in the Civilian Nuclear Sector," Oslo, Norway, June 17–20, 2006.
64. Russell Ball, "Use of LEU in the Aqueous Homogeneous Medical Isotope Production Reactor," RERTR 1994 International Meeting, Williamsburg, Virginia, October 1994; Russell Ball, "The Mo-99 Solution," *Nuclear Engineering International* 40 (December 1995), p. 42.
65. IAEA Consultancy on Utility of Homogenous Aqueous Solution Nuclear Reactors for the Production of Mo-99 and Other Short-Lived Radioisotopes, "Summary of Presentations, Discussions, Conclusions and Recommendation," June 20–22, 2007.
66. Russell M. Ball, V.A. Pavshook, and V.Ye. Khvostionov, "Present Status of the Use of LEU in Aqueous Reactors to Produce Mo-99," RERTR 1998 International Meeting, Sao Paulo, October 1998.
67. The ARGUS experiment also resulted in other useful medical radionuclides (strontium-90 and I-131), increasing the commercial prospects of the method. Roy Brown, president of Nuclear Medicine Solutions (formerly of TCI Medical), e-mail correspondence with author, April 3, 2007.
68. Although a full-scale pilot plant was never developed, there have been many short tracer experiments. Pablo Adelfang, "Symposium on Minimization of HEU in the Civilian Nuclear Sector," Oslo, Norway, June 17–20, 2006.
69. The National Nuclear Security Administration (NNSA) has supported Argonne research applicable to the development of a solution machine at B&W, which is coordinating its development effort with the national laboratory. In the past, NNSA also funded work at Kurchatov through the Initiatives for Proliferation Prevention (IPP) program. On the latter, see, Roy W. Brown, "Production of Medical Radionuclides at Russian Nuclear Institutes," presentation at Americas Nuclear Energy Symposium 2002, Miami, Florida, October 16–18, 2002, <anes.fiu.edu/Pro/s4Bro.pdf>.
70. It was noted at the IAEA consultancy on solution reactors that China and Russia are also pursuing radioisotope production at solution reactors. Consultancy participants included representatives of China's Medical Isotope Production Reactor at Chengdu as well as Russia's Kurchatov Institute and Institute for Physics and Power Engineering. See, IAEA Consultancy on Utility of Homogenous Aqueous Solution Nuclear Reactors for the Production of Mo-99 and Other Short-Lived Radioisotopes, "Summary of Presentations, Discussions, Conclusions and Recommendation."
71. W. Evans Reynolds, BWX Technologies, Inc., telephone interview with the author, April 2, 2007.
72. IAEA Consultancy on Utility of Homogenous Aqueous Solution Nuclear Reactors, "Summary of Presentations."
73. Ibid.
74. Official from the IAEA Nuclear Fuel Cycle and Materials Section (name withheld by request), e-mail communication with the author, March 8, 2008.
75. See, for example, presentations at RERTR meetings, as well as Luc Van Den Durpel, et al., "Myrrha: A Prototype Accelerator-Driven System," *Scientific Report 1997*, <www.sckcen.be/sckcen_en/publications/scientrep/97/E/E2.shtml>.
76. Ira N. Goldman, Natesan Ramamoorthy, and Pablo Adelfang, "Progress in the IAEA Coordinated Research Project: Production of Mo-99 Using LEU Fission or Neutron Activation," RERTR 2006 International Meeting, Cape Town, October 2006.
77. CRP T.1.20.18, "Developing Techniques for Small-Scale Indigenous Production of Mo-99 Using LEU or Neutron Activation: In Order [to] Assist Countries to Pursue Such Mo-99 Production," was initiated with

an IAEA Consultants Meeting in Vienna in November 2004 attended by participants from Argentina, Belgium, Canada, Netherlands, South Africa, and the United States, including representatives of the four major commercial producers of Mo-99. The CRP has received both DOE discretionary funding and money from the regular IAEA budget. The DOE made an extrabudgetary contribution to begin the CRP in 2005, and it has been supported from the IAEA regular budget since that time. Goldman, Ramamoorthy, and Adelfang, "Progress in the IAEA Coordinated Research Project: Production of Mo-99 Using LEU Fission or Neutron Activation."

78. Daniel Cestau, Ariel Novello, Pablo Cristini, Marcelo Bronca, Roberto Centurión, Ricardo Bavaro, Julián Cestau, and Eduardo Carranza, "HEU and LEU Comparison in the Production of Molybdenum-99," presentation at RERTR 2007 International Meeting, Prague, September 23–27, 2007.
79. Daniel Cestau, remarks on paper presentation at RERTR 2007 International Meeting, Cape Town.
80. George Vandegrift, Argonne National Laboratory, personal correspondence with author, March 27, 2008.
81. Manzini, "Producing Mo-99 from LEU Targets."
82. Ibid.
83. S. Balart, O. Calzetta, P. Cristini, J. Garces, A. J. Gauna, A. Gonzales, J.D. Hermida, E. Pasqualini, and H. Taboada, "Progress on RERTR Activities in Argentina," presentation at RERTR 2006 International Meeting, Cape Town, South Africa, October 29–November 2, 2006.
84. Taboada, remarks during paper presentation at RERTR 2006 International Meeting, Cape Town.
85. Ralph Butler, director, Research Reactor Center, University of Missouri-Columbia, e-mail correspondence with author, March 24, 2008.
86. Construction of a new building at MURR will cost about $35 million. MURR is seeking financing from the University of Missouri, DOE, and industry. With adequate funding, commercial operation could commence in four years. Currently, DOE is funding research and development efforts on a non-proprietary basis only. This includes some $600,000 in support for the MURR demonstration effort, from fiscal 2006 to fiscal 2008, as indicated in Daniel Horner, "Plans for US Isotope Reactors Carry Nonproliferation, Market Impacts," *Nucleonics Week*, February 14, 2008, pp. 3–5. It should be noted that the U.S. government currently will not fund any projects if they put other producers at a competitive disadvantage (even if they are in foreign countries or use HEU); thus, it is not clear that MURR can obtain the funding it needs to get operations started from the DOE.
87. Horner, "Plans for US Isotope Reactors Carry Nonproliferation, Market Impacts."
88. This point was made by MURR director Ralph Butler in Horner, "Plans for US Isotope Reactors Carry Nonproliferation, Market Impacts."