Executive Summary

The scientific literature contains case reports on >2,100 wounds contaminated with radionuclides. The vast majority of these reported wounds have occurred in the proximal and distal phalanges of workers in facilities that process plutonium. Since 1990 the use of depleted uranium (DU) in military munitions has resulted in combat wounds with DU shrapnel. In addition to contaminated wounds arising in industrial and military situations, medical use of radioactive material as a radiographic contrast agent [i.e., Thorotrast® (VanHeyden Company, Dresden-Radebeul, Germany), a colloidal suspension of thorium dioxide] has resulted in the development of granulomas (thorotrastomas) at injection sites, a type of foreign-body reaction complicated by the radiation delivered to the site.

By definition, a contaminated wound breaches the skin, which normally presents an effective barrier to the ingress of radioactive materials into the body. Skin is the largest organ of the human body, and its primary physiologic role is temperature regulation and maintaining homeostasis of body fluids and electrolytes. Human skin is a complex tissue, consisting of numerous distinct layers and types of cells. Immediately below the skin, the subcutis consists of loose connective tissue covering the muscle layer, with a variety of inorganic and organic chemicals and cells that affect the local retention and translocation of radionuclides introduced to it.

Although numerous biokinetic and dosimetric models for intakes of radionuclides by inhalation and ingestion have been published, a comparable consensus model for intake via contaminated wounds has not, even though the total amount of activity associated with a contaminated wound is typically much larger than that associated with worker exposures via inhalation or ingestion. Thus, in the mid-1990s the National Council on Radiation Protection and Measurements (NCRP) in collaboration with the International Commission on Radiological Protection (ICRP) established a scientific committee tasked with developing such a wound model.

Every contaminated wound presents the possibility of radionuclide uptake into the systemic circulation, with resulting doses to internal organs and tissues. Consequently, contaminated wounds
are almost always treated rapidly with excision of the wound site and administration of drugs to increase the excretion of radionuclides taken up into the systemic circulation, or to block their deposition in specific organs or tissues. Because of the paucity of data from humans who have had radionuclide-contaminated wounds but not had surgical or chemical decorporation, it was necessary to design and parameterize the wound biokinetic model using experimental animal data. For wound contamination with initially soluble radionuclides, data were found for 48 elements, which encompass all the groups of the periodic table except for the noble gases. The elements for which data were found and used in the wound model are shown in Figure ES.1. However, for colloids and particulate materials, much less information was available, mostly for uranium, plutonium, americium, and nuclear weapons test debris. Nevertheless, the data have been adequate to provide estimates of model parameters for relatively insoluble materials.

The NCRP wound model, shown in Figure ES.2, is a biokinetic model consisting of five compartments that comprise the wound site. Additionally, blood and lymph-node compartments receive radionuclides cleared from the wound site. The compartmental design was based on understanding of the physical and chemical properties of the deposited radioactive material, which can be soluble, a mixture of soluble and colloidal material, particulate or

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**Fig. ES.1.** Periodic table of the elements; the 51 elements for which data were available from experimental animal studies are shaded.
The intent was to provide a mechanistic basis for describing the biokinetics of radionuclides in wounds. Transfer of material between compartments is characterized using first-order rate constants, which empirically were found to be adequate for describing the data sets encountered to date.

Radionuclides introduced into the wound site as initially soluble materials enter the soluble compartment. Based on analysis of experimental data and aqueous chemistry considerations, two additional compartments were needed: (1) colloid and intermediate state (CIS) and (2) particles, aggregates and bound state (PABS). The initial partitioning of a radionuclide between the soluble and CIS compartments following injection is strongly influenced by aqueous solution chemistry, in particular, an element's tendency to hydrolyze at neutral pH. This affects its physicochemical state as well as its tendency as a charged molecule to bind locally to tissue molecules. For soluble materials, the principal clearance pathway from the wound site is via the blood. The amount of lymph-node clearance is dependent on the hydrolytic tendency of the material, which tends to produce more particulate characteristics.

Four default categories of soluble materials have been defined in the wound model: weak, moderate, strong and avid. Although these four categories were determined empirically based on wound retention times observed in the collected data from 70 experimental studies, the radioelements grouped roughly according to their
tendencies for hydrolysis at the neutral pH of a wound site as well as the tendency to form stable complexes in situ. These tendencies increase with increasing oxidation state as $1^- < 1^+ < 2^+ < 3^+ < 4^+$. Thus, the weak category contains complex oxo- and chloro-anions, monovalent and divalent cations. The moderate category contains chemical analogs of members of the weak category but with unique chemical properties that confer longer wound-site retention. The strong category consists mainly of trivalent elements such as yttrium, lanthanum and gallium, trivalent lanthanides and actinides including small masses of plutonium, and the avid category consists of tetravalent zirconium, tin, thorium, plutonium, and pentavalent protactinium.

Fragments and particles are both solid materials, which may be essentially pure substances like plutonium or DU metal, or oxides, or solid materials contaminated with radionuclides. For the purposes of the wound model, the difference between particles and fragments is that the latter are too large to be phagocytized. Colloids are most commonly formed as hydrolysis products of radioactive metals, and also have particulate properties. These materials are introduced into the wound model by direct injection into the CIS, PABS, or fragment compartments for colloids, particles and fragments, respectively. In general, one of the principal differences in behavior between initially soluble and insoluble materials is that the latter materials, being particulate with low solubility rates, can have significant clearance from the wound to lymph nodes; soluble materials typically do not. Additionally, wounds can contain significant masses of materials, which may also elicit inflammatory reactions in the wound tissue. As such, biological sequestration and capsule formation may occur, which provides a biological barrier to clearance from the wound site. These phenomena led to the creation of the trapped particles and aggregates (TPA) compartment.

During the parameterization of the wound model for insoluble materials, it became evident that the CIS compartment was not needed for particles and fragments. This is because the transfer rates from PABS and fragment compartments are so small that there is virtually no likelihood of having high enough concentrations of radioactive material in the soluble compartment such that hydrolysis/polymerization reactions would be probable. Therefore, CIS is not used for particles and fragments, which simplifies the modeling.

One of the important applications of the NCRP wound model relates to the need to interpret bioassay data from U.S. soldiers who were wounded with DU fragments during the Persian Gulf War.
Because the human data from medical follow-up of the wounded soldiers were too sparse for modeling, reliance was again placed on the use of experimental animal data. Using indirect data to estimate wound-site retention in rats implanted with DU metal wafers, the DU was shown to be retained in the wound for very long times (~300 y). Notwithstanding this long retention, measurable amounts of DU are still predicted to be excreted, and urine bioassay could potentially be used for intake estimation (Appendix D).

An example of the application of the wound model to aid in the interpretation of bioassay data, particularly for supplementing data from in situ wound measurements of DU, has been provided in Appendix D. Here the wound model was coupled with the uranium systemic biokinetic model of ICRP Publication 69 (ICRP, 1995a) and used it to predict the urine excretion patterns for uranium (or DU) for the three most likely default categories: weak, particle, and fragment. The urine patterns show that the greatest discrepancy in urine excretion rate occurs 1 d after exposure, in which the weak and particle fractions differ by more than three orders of magnitude, as do particle and fragment. Thus, knowing the physicochemical form of uranium or DU immediately after exposure will be very important in properly interpreting the urine excretion data. By ~100 d, the excretion rates tend to converge so that the differences become less important. Because the shapes of the urine excretion curves differ significantly, serial urine bioassays can be used to deduce which category of uranium in the wound is most reasonable. Similar predictions can be made for fecal excretion as well as uptake and retention in various systemic tissues and organs.

This Report provides guidance on appropriate bioassay measurements in cases of contaminated wounds and their interpretation. Equipment and methods for direct assessment of radioactive material in contaminated wounds are described, and tables of dose coefficients for skin (shallow) dose from surface contamination and local dose from embedded radioactive materials in a wound are provided. Dose coefficients and intake retention and excretion fractions have been derived for uranium by coupling the wound model with the ICRP systemic model for this element, and examples of their use are included. Development of these parameters for other radionuclides remain to be done; in the interim, tables of systemic dose from the complete uptake of various radioactive materials in a wound are also included by assuming that the radionuclide is intravenously (i.v.) injected in soluble form.

Finally, this Report provides detailed guidance on the medical management of contaminated wounds, using plutonium as an example. Treatment of life-threatening medical conditions always
takes priority over radiological assessment and treatment. Once the patient is stabilized, decontamination should proceed in the order of open wounds, body orifices, and then intact skin. Wounds should be copiously irrigated, and any foreign material removed and saved for radioassay. Excision of contaminated tissue may be performed, depending on the risk to important structures such as tendons and nerves, and the wound closed. In the case of contamination with transuranic radionuclides, chelation therapy with calcium- or zinc-diethylene triamine pentaacetic acid (DTPA) should be initiated, along with collection of urine and fecal samples for bioassay. Because the effectiveness of DTPA therapy decreases with time since uptake, initiation of therapy need not wait for complete radiological characterization of the contaminating radionuclide.

Guidance on the medical management of contaminated wounds is available from the Radiation Emergency Assistance Center/Training Site (REAC/TS), an emergency response asset of the U.S. Department of Energy (DOE) in Oak Ridge, Tennessee at any time by calling (865) 576-1005; basic information is available on the web at http://orise.orau.gov/reacts (ORISE, 2007). Another source of medical advice is the Medical Radiological Assistance Team at the Armed Forces Radiobiology Research Institute in Bethesda, Maryland [http://www.afrri.usuhs.mil (AFRRI, 2007)].