Needs for Radioactivity Standards and Measurements in Different Fields

This 1973 paper was written at a critical point in the development of applications of radioactivity and nuclear power, and it defined the needs of standards laboratories of the world for the remainder of the century. Although the paper [1] was co-authored by members of the Radioactivity Section, it was largely written by Wilfrid Mann and represents the fruition of his years of reflection on radionuclide metrology.

Standards are needed for radioactive materials to permit their accurate measurement for purposes of health, worker protection, and public safety. The National Bureau of Standards developed a program for standards and calibrations of radium-226 (1600 year half life) in the early part of the century [2,3], but this program was limited mainly to naturally-occurring radionuclides in the uranium and thorium series until the late 1940s. Following World War II, man-made radionuclides from reactors, linear accelerators, and cyclotrons became available for more routine uses in medicine, agriculture, and industry. The Bureau then began development of primary standardization techniques that could be applied to classes of radionuclides, such as pure beta-particle emitters [4], gamma-ray emitters, and alpha-particle emitters. In 1951, Lauriston S. Taylor envisioned a world-leadership role for NBS in radionuclide metrology and recruited Wilfrid Mann from the Chalk River laboratories in Canada. Throughout the 1950s and 1960s Mann built and expanded the Bureau's capabilities in radionuclide metrology [5], including techniques such as microcalorimetry, beta-gamma coincidence counting, gas counting, defined solid-angle alpha counting, and photon spectrometry. Metrology also required developing expertise in sample preparation, radiochemistry, isotope separation, sampling for environmental analyses, and measurement quality assurance. Thus, by the end of the 1960s NBS was ready to assume national leadership in measurements for radioactivity, and a timely report from the National Academy of Sciences [6] stressed the needs for radioactivity standards for public health, medicine, and nuclear science.

Needs for Radioactivity Standards was written just as the applications of radiopharmaceuticals in nuclear medicine were beginning a very rapid expansion. During the same period, the U.S. nuclear industry (and the industrialized world) were very positive about the prospects for cheap, abundant "atomic energy," and the utilities were building new nuclear power stations all over the country. Most of the 104 power reactors operating today were ordered during the 1970s. In each of the national standards laboratories, metrologists were considering how to meet the needs of these emerging technologies. This paper was the keynote presentation of the formative meeting of the International Committee for Radionuclide Metrology (ICRM). The paper both summarizes the status of radionuclide standards and explores the needs for standards, measurements, and traceability for the emerging fields of nuclear medicine and nuclear power. It provided a blueprint for national and international traceability.

In the first nine pages Mann laid the foundation for radionuclide metrology by introducing the concepts, terminology and historical developments of measurement standards and radioactivity standards. This entertaining and informative introduction was absolutely necessary to his later development of the concept of *traceability.* He points out that "criterion" and "standard" are synonyms in the English language. Criterion comes from the Greek, while standard is derived from the old French "estandart." It was a flag raised on a pole to indicate the rallying point of an army. Our battlefields of today have shifted from armed combat to economic warfare, and this sense of the word standard still resonates with U.S. industry. Derived standards of radioactivity differ from the base quantities of time, length, and mass in two important respects. First, radioactivity is an ephemeral quantity. The substance is decaying with some half life (a good example is the 6 hour half life ^{99m}Tc used in nuclear medicine) such that often the material no longer exists after the measurements are completed. In most cases, the standard must reside in a system (protocol, people, detector, and associated electronics) that can be used to measure a disintegration rate (activity) from first principles. Second, there are a few thousand radionuclides, and they are found in many matrices (gas, liquid, solid, soil, air filters), so that choices must be made on the select few nuclides and matrices for "national standards." *Needs for Radioactivity Standards* addressed the basic issues of identifying emerging technologies, ordering priorities, developing measurement quality assurance programs, and establishing traceability for key measurements at the national and international levels. Following the historical background, Mann gave special emphasis to needs for radiopharmaceuticals and for monitoring radioactivity in the environment.

In the area of radiopharmaceuticals, NBS was forging ties directly to the manufacturers and to professional medical groups, such as the College of American Pathologists (CAP), as well as to the Food and Drug Administration (FDA). This paper reported some of the first round-robins with clinical users for solution standards of the radionuclides ^{51}Cr, ^{59}Fe, and ^{131}I. These first sets of measurements were evaluated by the manufacturers, FDA, and the professional groups. It was readily agreed that such exercises were important to establish mutual trust between manufacturers and with the FDA drug reviewers. For the small group of manufacturers, equity-in-trade was an important consideration. Bulk radionuclides were routinely produced and sold as raw materials, and a few percent discrepancy in the assay between manufacturers could lead to thousands of dollars in disputed sales. Thus, a small expenditure on a common program at NBS would ensure that all parties were measuring the same quantity of activity. The FDA had a need to verify the calibrations of the suppliers as well. If they were in the same calibration program with the manufacturers, it would simplify their work on audits for quality control. However, the CAP did not have a mechanism for a long-term formal program in this area. Wilfrid Mann and Lucy Cavallo negotiated with the industry to set up a consortium of radiopharmaceutical manufacturers in North America to produce such standards on a continuing basis under the auspices of the Atomic Industrial Forum [7].

During the 1970s and 1980s this program addressed the critical needs of the industry for short-lived radionuclide standards for diagnostic imaging in nuclear medicine. One of the most difficult of these standardizations was the 6 hour half life ^{99m}Tc. It has long been the most important nuclide in terms of diagnostic imaging and accounts for over 90 % of the 13 million applications per year in the United States. Technetium-99m, a metastable form of technetium-99, is produced by a chemical extraction from a ^{99}Mo-^{99m}Tc generator, and the product must be purified to eliminate traces of the 67 hour parent nuclide. The logistical hurdles were also severe, as air cargo shipping of radioactive materials with a six hour half life before the days of rapid commercial air freight was problematic. Lucy Cavallo worked out the rapid procedures for chemical separations and source preparations for these two nuclides, and Robert Ayres and Alan Hirshfeld later reported on the standardization by $4\pi\beta$-γ coincidence counting [8]. These protocols for rapid standardization of high activity levels of radionuclides, developed by Lucy Cavallo and Ronald Collé, were adopted by industry and are still in use today. The program continued to expand and added approximately one new nuclide each year; at present, there are 28 radiopharmaceutical SRMs [9]. Ten of these 28 SRMs are distributed each year.

After 1987 the focus shifted towards radionuclides for use in therapy. Radionuclides have been used in therapy for many years, but in the recent past improvements in sealed source preparation and radiopharmaceutical targeting strategies have led to much greater use and, accordingly, demands for standards. An example of the continuing leadership of NIST in this area was the recent international workshop organized by Bert Coursey and Brian Zimmerman to identify the needs for standards for therapeutic nuclides [10]. The long-term impact of the NBS/NIST radiopharmaceutical standards program was evaluated recently in an economic impact study by Albert Link [11], who found that this program had a 97 to 1 benefit to cost ratio based solely on the economic benefits. The benefits in terms of improved quality of health care (better diagnostics, more effective therapies) to the U.S. public are even more significant than the economic benefits.

Prior to this 1972 conference, Mann had established competence at the Bureau on low-level radioactivity measurements, which are important for environmental monitoring. J.M.R. (Robin) Hutchinson had developed a number of low-level counting instruments [12] for gamma-ray and alpha-particle emitters, and Lloyd Currie had considered the statistics of low-level counting [13], with an experimental emphasis on ^{3}H and ^{14}C. In 1963, Currie transferred to the Analytical Chemistry Division and has achieved international prominence in atmospheric carbon measurements.

Needs for Radioactivity Standards reported on a new and very promising program for gamma-ray emission-rate SRMs for use in the emerging nuclear power industry. In early 1972, there were serious disagreements between the Atomic Energy Commission (AEC) and the new Environmental Protection Agency (EPA) on how to analyze liquid effluents from the six operating nuclear power stations. A meeting was organized at Oyster Creek nuclear power station in Tom's River, New Jersey, in February 1972 that included the AEC, the EPA, the New Jersey radiation health authorities, the utility, and Robin Hutchinson and Bert Coursey from NBS. It was decided that NBS would prepare mixed gamma-ray standard sources which would be used by all participants to calibrate their Ge(Li) spectrometers. Participants then received a set of blind samples from NBS which they measured as unknowns, and then reported their results to NBS. This very successful exercise led quickly to production of a set of Standard Reference Materials. The gamma-ray spectrum from one of these early SRMs is shown in Fig. 1. The nine principal lines

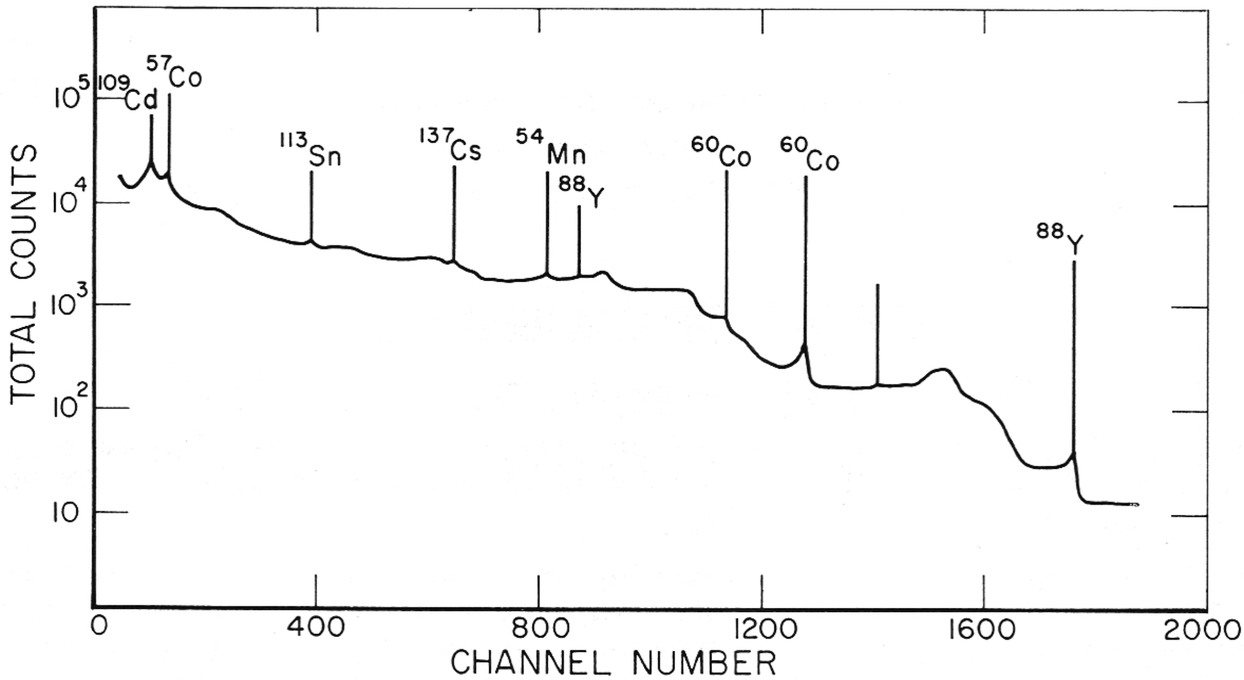

Fig. 1. Gamma-ray spectrum of a mixed radionuclide standard obtained with a 50 mL source positioned 2.54 cm from a 11 cm^3 Ge(Li) detector. Figure 9 in reference [1]. The lowest energy calibration point is the 88.0 keV gamma ray from ^{109}Cd , and the highest energy point is the 1836 keV gamma ray of ^{88}Y.

in the spectrum correspond to emissions from seven nuclides which were mixed in the proportions that the peak areas were approximately the same for a given counting time. This allowed the user to calibrate the system for all gamma-ray emitting fission and activation products at one time.

Hutchinson built on this example and organized a wider group of laboratories to consider the more difficult problems of environmental radioactivity in natural matrices. This led to a meeting of the International Committee on Radionuclide Metrology (ICRM) at Woods Hole, Massachusetts, in October of 1977. Participants considered the global problem of radioactivity in the environment and the standards that would be needed, as well as the required research in radiochemistry and the physics of low-level counting. Recommendations were made to produce standards of biological materials, soil, sediments, and waters, each to be certified for as many radionuclides as possible [14]. Hutchinson recruited Kenneth Inn, a young chemist from Arkansas, to take the lead on design of sampling and preparation of these natural matrix SRMs. One of the most popular of these was the Rocky Flats Soil SRM 4353 [15]. They quickly found that the man-made plutonium isotopes were not homogeneously distributed in the material (as the natural uranium and thorium were). This was due to the presence of hot particles in the soil from operations at the Rocky Flats plant in Colorado. In the past when Mann had encountered statistical problems in data analysis, he had turned to Bureau statisticians W.J. Youden and H.H. Ku. To help with the statistical analyses of these new data, Hutchinson and Inn turned to Walter Liggett and James Filliben. Their joint papers [15] provide a model for the interpretation of data from small samples near nuclear facilities (for example, swipe samples taken from nuclear facilities during International Atomic Energy Agency inspections).

Many of the NIST technical groups have to deal with the concepts of traceability to NIST. Mann recognized that this would be a critical problem for the nuclear industry, and that there would be slightly different requirements from the pharmaceutical industry, the nuclear utilities, the AEC (later DOE) laboratories, and those interested in environmental measurements. The direct and indirect traceability that he articulated in *Needs for Radioactivity Standards* had the common thread that one had to participate in a hierarchical measurements system which involved periodic blind testing of the laboratory's capabilities in order to assure traceability. The key federal regulators—the FDA for pharmaceuticals, the EPA for the environment, and the

Nuclear Regulatory Commission (NRC) for the power stations—accepted these definitions from NBS and worked with NBS and the user communities to set up measurement assurance programs and, later, accredited calibration laboratory programs to meet the common needs of the users and the regulators, with NBS serving as an impartial third party to prepare the SRMs and solve critical measurement problems. This paper has been widely cited in the U.S. and the international community for the past quarter century as the White Paper on achieving traceability in radioactivity measurements. A few of those present at that first meeting at Oyster Creek in 1972 were on the ANSI Subcommittee N42.2 that prepared an American National Standard—*Traceability of Radioactive Sources to the NIST and Associated Instrument Quality Control* [16].

Wilfrid Mann was born in Ealing in the United Kingdom on August 4, 1908. He received his Doctorate in Physics from Imperial College of Science and Technology in London in 1937 and did postdoctoral work during the 1930s in Copenhagen and Berkeley. While at Berkeley he worked with E. O. Lawrence on the cyclotron in the Radiation Laboratory and was the discoverer of the radioisotope ^{67}Ga, which is still in use in nuclear medicine [17]. His supervisor at Imperial College was G. P. Thompson, the British physicist in charge of the Tube Alloys project during the war years (the British nuclear program which was incorporated into the Manhattan Project). He had Mann assigned to the British Embassy in Washington. His interactions with his supervisor at the Embassy, Kim Philby, and another coworker there, Guy Burgess, gained Wilfrid considerable notoriety when the two were implicated in one of the biggest spy scandals of the century. In memoirs written much later [18], Wilfrid was able to show that he was not involved in nuclear matters while stationed in Washington and could not have taken part in their nefarious activities. Following his tour in Washington, Thompson assigned Mann to work with Sir John Cockcroft at the Canadian nuclear facilities at Chalk River. At this point he began careful measurements to intercompare the national radium standards of the UK, Canada, and the United States. This work was continued when he came to NBS in 1951 as the head of the Radioactivity Section. For the next 40 years Wilfrid Mann was one of the most influential researchers in his field. At intervals of a few years over this period of four decades Mann prepared books, handbooks, and extended monographs to describe completely the current state of the art in radionuclide metrology. The first of these were NBS Circular 594 [4] in 1958 and NBS Handbook 80 in 1961 [19]. These were followed by a book *Radioactivity and Its Measurement* with Samuel Garfinkel in 1966 and an expanded second edition with Robert Ayres in 1980 [20]. Following his retirement from NBS in 1980, he collaborated with Albrecht Rytz and Alfred Spernol on *Radioactivity Measurements: Principles and Practice* [21]. Perhaps his most lasting contribution to metrology was the monumental task of editing *A Handbook of Radioactivity Measurements Procedures* [22], NCRP Handbook 58. The first edition was published in 1978; the second in 1985 sold more copies than any other handbook of the NCRP and set out the principles of radionuclide metrology for a generation.

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