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General Schedule
Position Classification Standards

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POSITION CLASSIFICATION STANDARD FOR PHARMACOLOGY AND TOXICOLOGY SERIES, GS-0405/0415

Workforce Compensation
and Performance Service

Theodore Roosevelt Building 1900 E Street, NW Washington, DC 20415-8330 Classification Programs Division

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SERIES DEFINITIONS

PHARMACOLOGY SERIES GS-0405

This series includes positions the duties of which are primarily to administer, advise on, supervise, or perform research, analytical, advisory, or other professional and scientific work in the discipline of pharmacology. Such work requires the application of a knowledge of the history, sources, physical and chemical properties, biochemical, toxic, and physiological effects, mechanisms of action, absorption, distribution, metabolism, biotransformation and excretion, and therapeutic and other uses of drugs.

Pharmacology:

(1) involves the many aspects of the action of drugs or similar agents on living systems and their constituent parts, ranging from the intermolecular reactions of chemical compounds in a cell with drugs, to the evaluation of the effectiveness of a drug or agent in the treatment of human disease; and

(2) requires intensive preparation and training in organic chemistry, biochemistry, physiology, and pharmacology; the application and interpretation of a full range of methods, procedures, and techniques relative to the action of drugs or similar agents, but does not require full professional training in medicine or veterinary medicine.

TOXICOLOGY SERIES GS-0415

This series includes positions, the duties of which are primarily to administer, advise on, supervise, or perform research, analytical, advisory, or other professional and scientific work in the discipline of toxicology. Such work involves the study of adverse effects of chemical substances or similar agents on living organisms and/or the environment, and the assessment of the probability of their occurrence under specified conditions of use or exposure.

Toxicology:

(1) involves the study of the interaction of chemical and physical agents and biological systems, the exploration of the nature and mechanisms of adverse reactions, and the assessment of the likelihood that adverse effects will occur; and

(2) requires the application of scientific knowledges including, but not limited to, pathology, anatomy, chemistry, biochemistry, microbiology, physiology, pharmacology, toxicology, and materials sciences (e.g., as they pertain to the interrelationships of composition, structure, and properties), but does not require full preparation for practice in any one of those disciplines, or full professional training in medicine or veterinary medicine.

This standard applies to positions in two series: the Pharmacology Series, GS-0405, and the Toxicology Series, GS-0415. It provides occupational background information intended to clarify the intent and coverage of the series definitions, although it does not include grade-level criteria.

The Pharmacology Series, GS-0405, series-coverage standard cancels and supersedes the standard for the Pharmacology Series, GS-0405, issued in June 1965. It revises the concept and coverage of the former Pharmacology Series, GS-0405, to exclude positions primarily concerned with toxicology related functions and activities.

The Toxicology Series, GS-0415, is a new series coverage standard. It also provides occupational information intended to clarify the intent and coverage of the series definition. Many positions that now fall within this series were formerly classified in the Pharmacology Series, GS-0405, issued in June 1965. Other positions now covered by this series were classified in series including the Biology Series, GS-0401, the Microbiology Series, GS-0403, the Physiology Series, GS-0413, and the Chemistry Series, GS-1320.

EXCLUSIONS

Scientists working in related disciplines or fields of science often perform work similar to that performed by a pharmacologist or a toxicologist; however, because of the nature of the paramount qualifications required and the primary emphasis of the work, positions in these disciplines or scientific fields are *excluded* from the Pharmacology Series and Toxicology Series. This similarity of work is most likely to occur in the professional series listed below:

1. Positions primarily concerned with the development, application, and use of chemical, physical, and biological controls for insects, birds, mammals, and other economically or medically important forms of life, are classified in the Entomology Series, GS-0414, or the Wildlife Biology Series, GS-0486. While these controls or agents often are harmful or toxic to living organisms, and the entomologist or wildlife biologist may need to determine the effect of specific agents on such organisms, this is not, as would be the case in the work of the pharmacologist or the toxicologist, the primary purpose of the work.

2. Positions primarily concerned with the properties, compounding, and dispensing of drugs are classified in the Pharmacist Series, GS-0660. Such work involves the application of a knowledge of pharmacology (but not of the full range of methods, procedures, and techniques characteristically applied in pharmacology work), and usually requires that the incumbent be properly licensed to practice pharmacy. Some pharmacist positions involve the evaluation of drug proposals submitted by private industry and the surveillance of marketed drugs for safety and efficacy. However, pharmacy work typically is more concerned with the properties, preparation, and dosage of approved drugs than with the development of new drugs and their eventual use in the practice of medicine.

3. Where full professional preparation in medicine, and a license to practice medicine or psychiatry is a primary requirement, the work is classified in the Medical Officer Series.

4. Positions that have a *paramount* requirement of full professional preparation in veterinary medicine are classified in the Veterinary Medical Science Series, GS-0701.

5. Positions primarily concerned with occupational health hazards to which workers are exposed (e.g., excessive amounts of toxic or irritant chemicals found in the workplace and with their methods of control), are classified in the Industrial Hygienist Series, GS-0690. In general, the industrial hygienist is concerned with controls to reduce or eliminate hazardous exposure conditions in the workplace, while the toxicologist is concerned with the study of the adverse effects of chemicals on living organisms and/or environment.

6. Positions concerned with the study of ecological relationships, the interrelationships of organisms with each other, with their physical and chemical environment and with society, are classified in the Ecology Series, GS-0408. Pesticides testing and control generally are the concern of ecologists in the area of environmental protection together with energy source and technology analysis and development. Ecologists test pesticides in conjunction with determining pollution levels and predicting the impact of planned construction primarily as they relate to the assessment of changes in ecosystem processes.

7. Positions concerned with protecting or improving the natural resources of air, land, and water in order to provide a clean and healthful environment are classified in the Environmental Engineering Series, GS-0819. While the toxicologist is concerned with air, water, and soil pollution as they relate to assessment of the hazards of exposure to chemical or physical agents, the environmental engineer typically is concerned with the facilities or systems of industrial or municipal plants to the extent that they affect environmental resources.

8. Positions classified in the General Biological Series, GS-0401, the Microbiology Series, GS-0403, the Zoology Series, GS-0410, the Physiology Series, GS-0413, the Genetics Series, GS-0440, the Physics Series, GS-1310, and the Chemistry Series, GS-1320.

Distinctions between pharmacologist or toxicologist positions and others involving closely related disciplines depend upon the primary purpose and emphasis of the work, the area of focus, the methodology and approach involved, the career patterns, and the requirement for the application of a full range of respective pharmacological or toxicological knowledges and skills.

DISTINGUISHING BETWEEN THE PHARMACOLOGY DISCIPLINE AND THE TOXICOLOGY DISCIPLINE

Pharmacology and toxicology have a common origin, but their emphasis has become sufficiently diverse so that they now are two fields of effort and should be classified separately. Pharmacology and toxicology are recognized as autonomous scientific disciplines -- not as subcomponents of each or any other restricted discipline. Basic research concerning the identification and clarification of the mechanisms of chemical pathways and metabolism is fundamental to the achievement of an understanding of the phenomena involved in both toxicology and pharmacology; however, it is appropriate to consider the two as different and discrete disciplines.

Toxicology and pharmacology are closely related disciplines dealing with the responses of biological systems to chemicals and other substances, both naturally occurring and synthetic. These disciplines differ, however, in both focus and scope.

The following outline indicates certain points of differentiation between pharmacology and toxicology:

PHARMACOLOGY	TOXICOLOGY
(1) Focuses on the testing, review, and evaluation of substances of overall biological effects, mechanisms of action, and potency for the ultimate goal of applied usefulness. Concentrates on processes or mechanisms of action.	(1) Focuses on the testing, review, and evaluation of substances for the purposes of identifying deleterious effects. Generally focuses on impact, or outcome.
(2) Is ultimately concerned with the effects of drugs. The pharmacologist's efforts include development of practical, efficacious, therapeutic agents to be administered with purposeful intent.	(2) Studies the effects produced by overdosage or possible adverse effects unrelated to therapeutic action. The toxicologist also is concerned with substances, other than drugs, that are expected to have beneficial effects (e.g., asbestos for insulation), yet produce unintended negative consequences.
(3) Is broadly concerned with the qualitative and quantitative relationships between substance (dose) and response (effect). Pharmacologists use the substance either for clarifying physiological mechanisms, or for alterations of the physiological state (stimulation or depression).	(3) Is broadly concerned with the qualitative and quantitative relationships between substance (dose) and response (effect). Toxicologists are concerned with noxious or adverse responses of all chemical substances which, in turn, calls for both an interest in and a familiarization with pathological processes.
(4) Purview encompasses beneficial effects of drugs and other substances. For example, substances investigated by the pharmacologist may be identical drugs to those investigated by the toxicologist for human or animal consumption for therapeutic uses. The pharmacologist, however, focuses on beneficial, therapeutic effects (while being conscious and knowledgeable about dose limits, toxicity, noxious effects due to overdose, exaggerated pharmacological effects, as well as side effects), and the dosage ranges, mechanisms of action, and particular impact on systems of the body.	(4) Considers the interplay of all toxic substances with biological systems. For example, substances investigated by the toxicologist may be identical drugs to those investigated by the pharmacologist for human or animal consumption for therapeutic uses. However, the toxicologist normally is concerned with all substances that may produce toxic effects, e.g., materials that may be hazardous without any necessary intended beneficial effect, where the time period, nature, and extent of exposure may be unknown. Investigates the source of the observed effect and assesses the nature, magnitude, and onset of the risk involved.

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PHARMACOLOGY	TOXICOLOGY
(5) Functional and organizational differences frequently exist in the Federal service, e.g., effects of drugs on bodily functions, or metabolic alterations associated with therapeutic drugs tend to be the province of pharmacologists.	(5) Functional and organizational differences frequently exist in the Federal service, e.g., toxicologists are concerned with hazards associated with chemicals in the workplace, newly introduced toxic substances, environmental measurements, and bioassays of environmental agents.
(6) Concerned with the identification of substances and the evaluation of dose levels most appropriate to the prevention and alleviation of disease. Concerned with drugs and certain compounds important to the physician in the treatment of disease/ illness or management of patients.	(6) Concerned with acute, subacute, and chronic toxic responses in biological systems. Concerned and interested somewhat with effects of drugs, but less so for the therapeutically useful drugs or their therapeutic efficacy.
(7) Long-term, chronic effects are of interest to the pharmacologist; however, his/her concern with these and the evaluation and monitoring of them generally are narrower than concerns of the toxicologist.	(7) More concerned with acute or long-term, chronic effects, real or hypothetical, of substances deliberately released into or known to be present in environmental situations, or those that accidentally or incidentally may constitute recognized or unrecognized exposure risks.

The toxicologist is concerned with materials that may be hazardous and without any necessary direct health benefit (in contrast to drugs) to the individual or living organism at risk as a result of their use. The primary emphasis in delineating a toxicologist's approach to such materials lies in the areas of:

-- dose-response relationships;

-- the effects and mechanism of effects of repeated exposures and delayed injuries;

-- the study of mechanisms to develop a scientific basis for prediction of potential injury; and

-- toxicology as a basic bridge between biomedical sciences and the chemical sciences.

It is recognized that many toxicologists essentially have emerged from strong pharmacological backgrounds, and some phases of toxicology (e.g., clinical, biochemical, neurotoxicological, behavioral) are closely tied to pharmacology.

Certain concepts developed in pharmacology are deemed essential for understanding the chemical interactions with the biological systems which result in deleterious responses. Such concepts developed in pharmacology include those such as the dose-response relationship, the time-response relationship, the disposition of chemicals in the organism, pharmacokinetics, metabolism, and chemical interactions -- all necessary concepts which must be mastered by the toxicologist. While pharmacology usually is associated with the study of drugs used for therapeutic purposes, the concepts developed in this discipline have applications when dealing with other chemical substances used in other types of environments for different purposes. It is these concepts which should be stressed, not the discipline per se, in the collection and application of knowledge.

PHARMACOLOGY SERIES
BACKGROUND

Pharmacology deals with the characteristics of drugs and related substances; the metabolic interaction of these with different organisms, organ systems, tissues, and their parts; the chemical and pharmacodynamic properties of specific drugs or agents individually, in combination, and comparatively (when administered to different species of animals); drug efficacy and safety; and the application or impact of different drugs or substances to human or veterinary medicine, or their effect on humans in general.

National interest focuses on the probable conquest and prevention of major diseases by drug therapy; on the efficacy, safety, and cost of new and old drugs; and on the unresolved problems of drug and alcohol abuse.

Concern for the effects of drugs is the primary function of the discipline of pharmacology, which concentrates on effects of drugs and related substances. Pharmacology is concerned primarily with dose response, metabolism, distribution, elimination, organ systems, mechanisms of action, and intended short-term and long-term effects of a variety of therapeutic chemicals. While the pharmacologist is knowledgeable about toxic impact of a given substance, the focus of interest is on therapeutic use and range of dosage, by various routes of administration and known exposures, the reversible or irreversible nature of the impact on particular organ systems (such as liver, kidneys) and the mechanisms of action. Pharmacologists undertake or contribute to the development of practical, efficacious, therapeutic agents to be administered with purposeful intent to humans or animals with diseases or illnesses.

Pharmacologists develop or contribute to the development of, for use in humans, potent chemical agents including, but not limited to, cardiac stimulants, antibiotics, and antidiabetic, antihypertensive and anticancer drugs. Benefits of a drug may be accompanied by detrimental side effects, often creating unprecedented problems; therefore, new drugs, highly selective in their beneficial effects, are required. The pharmacologist seeks to learn more about the interaction of drugs with specific receptors in the cell. Pharmacologists determine the effects of drugs on all organ systems including the cardiovascular, pulmonary, central nervous, digestive and excretory, and autonomic nervous systems, as well as possible drug interactions.

Major aspects of pharmacology considered in the scientific approaches to pharmacological studies include the following:

Pharmacokinetics -- deals with the absorption, distribution, bioaccumulation, biotransformation, and excretion of drugs. These factors, coupled with dosage, determine the concentration of a drug at its sites of action, and, therefore, the intensity of its effects as a function of time. Many basic principles of biochemistry and enzymology and the physical and chemical properties that govern the active and passive transfer and the distribution of substances across biological membranes are applied to the understanding of this aspect of pharmacology. Pharmacokinetics may be required for establishing safety to the target species when the drug is efficacious and an adequate margin of safety has not been established. Pharmacokinetics and drug metabolism

studies are made on animal species as well as humans. These data are used in the planning of certain preclinical investigations and of the dosage regimen in the clinical protocol.

Pharmacodynamics -- includes the study of the biochemical and physiological effects of drugs and their mechanisms of action. Pharmacodynamics borrows from both the subject matter and the experimental techniques of physiology, biochemistry, cellular and molecular biology, microbiology, immunology, genetics, and pathology. Primary attention is focused on the characteristics of drugs. Another ramification of pharmacodynamics is the correlation of the actions and effects of drugs with their chemical structures. Such structure-activity relationships often lead to the development of better drugs.

Clinical pharmacology -- emphasizes the use of drugs in humans and animals, as the effects of drugs often are characterized by significant interspecies variation, which may be further modified by disease, age, and sex. While certain animal tests can adequately screen drugs for psychoactivity, some drug effects on mood and behavior can be adequately studied only in humans. However, as technical, legal, and ethical considerations limit pharmacological evaluation in humans, the choice of drugs must be based in part on their pharmacological evaluation in animals. Consequently, significant knowledge of animal pharmacology and comparative pharmacology is necessary in deciding the extent to which claims for a drug based on studies in animals can be reasonably extrapolated to humans. (Note: Work where the scientist is responsible for the actual administration of drugs to patients typically is excluded from coverage of this standard.)

Pharmacotherapeutics -- deals with the use of drugs in the prevention and treatment of disease. From the standpoint of the scientist studying the therapeutic uses of a drug, the selectivity of its effects is a primary characteristic. Drug therapy is rationally based on the correlation of the actions and effects of drugs with the physiological, biochemical, microbiological, immunological, and behavioral aspects of disease. Pharmacodynamics provides an opportunity for this correlation during the related scientific studies.

REQUIRED KNOWLEDGES

The acquisition of required knowledges results from cross-disciplinary training in the biological and physical sciences, intensive preparation and training in chemistry, biochemistry, physiology, and pharmacology, and, to an increasing degree, additional preparation in such areas of science as biophysics, microbiology, and genetics, as well as mathematics and statistics.

Pharmacology is multidisciplinary in nature requiring preparation and training in the preceding areas of study along with the application and interpretation of a full range of methods, procedures, and techniques relative to the action of drugs. The work performed by a pharmacologist requires a knowledge of experimental design, and behavioral and pharmacological research techniques.

Pharmacologists are concerned with the most intricate processes of life -- the cellular, molecular, and behavioral responses to drugs and similar materials in a living organism. They apply knowledge of the source, chemical and physical properties, action, absorption, distribution, metabolism, excretion, and use of drugs and related chemicals.

Scientists trained in other scientific disciplines typically work with pharmacologists in study teams/groups or apply their specific knowledge of science in the solving of particular problems. Such a study team/group may comprise, for example, organic chemists, biochemists, physiologists, pathologists and, sometimes, biophysicists and microbiologists. Final evaluations take into consideration the findings of these various scientists, with the final action/decision taken usually based on the recommendations of the chemists, pharmacologists, and medical officers who have reviewed these evaluations.

The pharmacologist uses experimental techniques from many different disciplines to determine:

-- the molecular mechanism and site of action of a drug;

-- the relation between dose and effect and between chemical structure and effect;

-- how the drug is absorbed, distributed, biotransformed, and eliminated;

-- the adverse as well as the beneficial effects of a therapeutic substance;

-- the drug safety based on the effective dose compared with the toxic dose.

MAJOR DUTIES AND FUNCTIONS

Pharmacologists conduct basic investigations of the reciprocal interactions between drugs and living systems; contribute to basic and applied research to create new therapeutic agents to cure and alleviate disease and improve life; and/or engage in clinical studies that assess the therapeutic effectiveness of drugs in humans.

Pharmacologists in the Federal Government participate in a broad spectrum of work assignments. They work in laboratories and offices of Federal Government agencies concerned with basic research, with the regulation of commerce, and with the protection of public health and safety. They examine efficacy, toxicity, and other requirements established by legislation. The work of the pharmacologist also may be concerned with determining whether a drug meets "approved standards." In many regulatory cases, the approved standard is in the imprecise lay language of the enabling legislation, and the pharmacologist must identify the data, through translation of this language, in order to provide the proper assessment.

Pharmacologists review and evaluate scientific data submitted by industry to determine the meaning of the data; and whether the data are valid and support the efficacy, purity, and potency of a drug or product. Other types of positions are research or laboratory oriented, conducting research to develop new scientific information that will serve as a basis for regulatory decisions made by review scientists.

Pharmacologists also may serve as project officers on contracts awarded universities or organizations in the private sector. This contract work provides data the pharmacologist needs to function as a regulator with expertise in pharmacology. Responsibilities include establishing work statements and objectives based on knowledge of the state-of-the-art and agency needs. Duties involve week-to-week oversight of the work and planning for testing and/or evaluation profiles that will best yield the desired information and provide needed assessments (e.g., abuse potential of drugs).

Pharmacological research encompasses investigations in many different areas and, within a particular area, involves studies at the molecular, cellular, and organ level, and also with the intact living animal. Pharmacologists generally have some familiarity with most, if not all, specialty fields, enabling them to adopt appropriate new techniques when necessary in investigative activities. Most pharmacologists, however, carry out research at one of several levels in biological activity. Specialty areas in pharmacology typically focus on organs and systems of the human body, such as the liver or kidneys, and the central nervous, respiratory, cardiovascular, and endocrine systems. Examples of specialty areas include:

Molecular pharmacology -- considers the biochemical and biophysical characteristics of interactions between drug molecules and those of the cell -- a branch of molecular biology applied to pharmacological questions.

Biochemical pharmacology -- uses the methods of biochemistry, cell biology, and cell physiology to determine how drugs interact with, and influence, the chemical mechanisms of the organism. Examples of therapeutic benefits derived from biochemical pharmacology include the

use of drugs as probes to discover new information about biosynthetic pathways and their kinetics, and investigation of how drugs can correct biochemical abnormalities that are responsible for human illness.

Neuropharmacology -- studies drugs which modify the functions of all parts of the nervous system including the brain, spinal cord, and the nerve fibers which communicate with all parts of the body. Neuropharmacologists study drug actions for a variety of reasons, including:

(a) the probe of neurochemical disorders underlying specific disease states to find new ways to use drugs in the treatment of disease;

(b) alternately, the study of drugs already in use to determine more precisely the neurophysiological or neurobiochemical changes which they produce; and

(c) the use of drugs as tools to clarify basic mechanisms of brain function or to provide clues to the nature of the disease processes.

Behavioral pharmacology (psychopharmacology) -- studies the effects of drugs on the behavior of intact organisms, generally rats, mice, monkeys, or other species of laboratory animals. Research covers the gamut of behavior, objectively and quantitatively measured, to discover mechanisms by which drugs alter functions of the central nervous system. The discipline of psychopharmacology includes studies of abuse potential and the assessment of abuse potential and dependence liability for purposes of potential scheduling under the current Controlled Substances Act.

Cardiovascular pharmacology -- concerns the effects of drugs on the heart, the vascular system, and those parts of the nervous and endocrine systems that participate in regulating cardiovascular function. The cardiovascular pharmacologist contributes to development of clinically useful drugs for the treatment of various related diseases; also to uncovering new knowledge about the mechanisms by which certain disease processes alter cardiovascular function. Experimental approaches in this aspect of pharmacology may include research on humans and/or animals with and without cardiovascular disease, and on isolated tissues, individual cells, or subcellular units.

(Note: Work where the scientist is responsible for the actual administration of drugs to patients normally is excluded from coverage of this standard.)

BASIC QUALIFICATION REQUIREMENTS

Working in pharmacology requires in-depth professional education and experience in pharmacology and knowledge and skill in the application and interpretation of the pharmacological methods, procedures, and techniques pertinent to the investigation and development of drugs and to the action of drugs on living systems and their constituent parts.

The required knowledge and experience are of such an advanced nature that most positions require a doctorate in pharmacology or equivalent education and training. However, some developmental or limited assignment positions may be filled by candidates with less formal education and experience.

TITLES AND SPECIALIZATIONS

Separate titles have not been established for research and nonresearch positions as there generally are no significant differences in the qualification requirements for these positions. "Pharmacologist" is the authorized title for nonsupervisory positions classified in this series. The title "Supervisory Pharmacologist" is to be used for those positions that involve supervisory duties and responsibilities that meet or exceed the criteria for evaluation as a supervisor in the General Schedule Supervisory Guide.

Pharmacologists typically specialize in one or more aspects of their broad field of work. A great many specialty areas can be identified on the basis of function, subject matter, or area of application, each having a valid specific use for some personnel management purpose. Because of the wide variation in the nature and extent of the specialty areas, it is not practicable to reflect these in class titles. In consideration of the differing needs of the agencies and the effect of changes in programs and in natural, applied, and experimental sciences, the establishment of such specialized titles would needlessly complicate the process of personnel management.

The specialty areas may be considered in selective placement and other personnel actions even though they are not specified in the titles.

EVALUATION NOTES

This series-coverage standard does not include grade-level criteria. Research positions should be evaluated by reference to the Research Grade Evaluation Guide. Positions primarily concerned with evaluating and recommending approval of pharmacological related research grants and contracts should be evaluated by reference to the Research Grants Grade Evaluation Guide. The General Schedule Supervisory Guide should be used to evaluate supervisory positions. Other types of pharmacology positions should be evaluated consistently with published standards by cross series comparison. Among the published standards that might be used as cross references are those for the Microbiology Series, GS-0403, and the Chemistry Series, GS-1320.

TOXICOLOGY SERIES
BACKGROUND

The Society of Toxicology has defined toxicology as "the science which studies the adverse effects of chemicals on living organisms and assesses the probability of their occurrence." Some of the important concepts of activity in the field, e.g., risk assessment, are embodied in the definition of a toxicologist as "a scientist who applies expert knowledge to the study of adverse effects of chemicals on living organisms and to the assessment of the probability of their occurrence." The main thrust of toxicology research, therefore, is to understand mechanisms of chemical injury and to apply that knowledge to risk assessment. Toxicology also has been described as the study of the harmful actions of chemicals on biologic tissue, involving an understanding of chemical reactions and interactions as well as an understanding of biologic mechanisms.

Further, there are a number of common elements to modern toxicology, including the following required interrelated elements:

(1) there must be a chemical or physical agent capable of producing a response;

(2) there must be an identifiable biologic system with which the agent may interact to produce a response;

(3) there must be a response that can be considered deleterious to the biologic system; and

(4) there also must be a means by which the agent and the biologic system are permitted to interact.

A central element of toxicology is the delineation of the safe use of chemicals. For example, major concerns of a toxicologist's discipline include the following considerations and measures:

-- *hazard* -- the probability that injury will result from a chemical under specific conditions;

-- *safety* -- the practical certainty that injury will not result from use of a substance under specified conditions of quantity and manner of use;

-- *toxicity* -- the capacity of a substance to produce injury.

In the development of toxicology as a discipline, the essential ingredient is the "why" of the toxic response. Basic research typically is necessary to determine how noxious substances gain access to the biologic system and arrive at a site of action and define the molecular events underlying the changes that occur.

Such work requires the application of a broad knowledge of the system responses of the whole organism and the interaction effects between subsystems of the organism. Using these knowledges, the toxicologist then designs and/or reviews protocols for the safety or hazard

evaluation of compounds with poorly known or unknown toxicologic characteristics. These compounds or substances include agricultural chemicals, industrial materials, household products, drugs in both medical and nonmedical usage; food components, additives, and contaminants; cosmetic formulation and ingredients; pollutants in the environment from all sources; radiation, heat, noise; and endogenous and exogenous biotoxins.

Toxicology also involves the study of long-term, chronic effects, sometimes relating to low levels of exposure and the detection of impact, interspecies interpretation based on studies on animals, and epidemiological studies involving humans and animals.

Passage of various major Federal laws requires that all potentially hazardous substances to which the public is exposed be evaluated for safety. It is estimated that over two million chemical compounds currently exist. Over 50,000 chemical substances are used in commerce and manufacturing and thousands of new ones are introduced every year.

With the introduction of numerous Federal laws aimed at protecting the environment, safeguarding employees in their workplace, and protecting consumers against hazardous household products, agencies of the Federal Government have assumed broad regulatory and evaluation responsibilities to provide prevention health measures and deal with the thousands of compounds and substances that must be evaluated. These regulations mandate extensive laboratory evaluation, and a major role of a toxicologist is to identify relationships between exposure to chemical agents and their short-range and long-range effects on human and animal health and populations. The toxicologist's responsibility begins when a compound is synthesized or proposed for use. Toxicologists are charged with the responsibility for characterizing the responses produced following exposure to a given compound and the level of exposure that can be tolerated without adverse reactions. Levels of exposure in terms of dosage or concentration and duration usually determine whether injury will occur -- injury which may be in the form of irritation, sensitization, organ dysfunction, fetal malformation, genetic damage, cancer, or death.

In many instances, the results derived from experimental animal studies provide a basis for predicting whether a compound can safely be made available for use in humans or animals, or safely introduced into the environment where humans or plant or animal species may be exposed to it. The information obtained by toxicologists typically provides the basis for making decisions which balance the benefits derived against the hazards presented.

While toxicologists are concerned with the scientific principles underlying actions of substances, their primary focus is on the whole organism. In this context, the toxicologist is concerned with adverse effects which may persist for prolonged periods after exposure to the toxic substance has ceased. Responses to a toxic agent include possible synergistic interaction effects between subsystems of the organism which may be manifested at various stages in its development. These effects can occur in the embryo, fetus, neonate, juvenile, mature organism stages and in subsequent generations. Thus, the toxic impact on humans and other animals and other organisms may be unknown for many years.

The work of a toxicologist usually is concerned with:

-- the investigation of chemical substances or similar agents and physical phenomena to determine their actual or potential injurious effect on organisms;

-- the design, development, validation, and/or review of research protocols for hazard evaluation of compounds of poorly known or unknown characteristics; and

-- decision making based on predictive evaluations of probable adverse effects, including possible carcinogenic, mutagenic, teratogenic, or other effects, to estimate the relative hazard and environmental and probable metabolic fate of substances.

This work may be performed at any stage in the use of the material and may involve premanufacturing review. Inquiries also may be conducted to investigate hazardous situations long after use of the substance has terminated or in subsequent generations.
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THE ROLE OF THE TOXICOLOGIST

The toxicologist usually is specially trained to examine the nature of adverse effects of chemicals or other substances on living organisms and to assess the probability of their occurrence under specified conditions of use or exposure. The variety of potential adverse effects and the diversity of chemicals present in our environment combine to make toxicology a broad area of scientific inquiry. Toxicologists usually concentrate upon one of the three main categories of toxicology as defined below:

The laboratory toxicologist -- directly concerned with toxicity testing. The appropriate toxicity tests in experimental animals are designed to yield information that can be used to evaluate the risk posed to humans, animals, and/or environment by exposure to specific chemicals. Their concern generally relates to effects on humans and animals as in the case of drugs or food additives. Toxicologists may be concerned not only with risks posed by chemicals (insecticides, herbicides, solvents, etc.) to humans, but also with potential effects on animals, fish, birds, or plants.

The research toxicologist -- concerned with clarifying the mechanisms by which chemicals exert their toxic effects on living organisms. Results of these studies often lead to sensitive predictive tests useful in obtaining information for risk assessment, help develop chemicals that are safer, or suggest rational therapy for toxic symptoms. In addition, toxicological studies also may contribute to the knowledge of basic physiology and biochemistry. These toxicologists usually are active in Federal Government research institutes.

The regulatory toxicologist -- responsible for deciding, on the basis of data provided by the laboratory toxicologist, whether or not a drug or chemical has a low enough risk to be marketed for the described purpose. For example, the Food and Drug Administration currently is responsible for evaluating the safety of existing, along with proposed, drugs, food additives, and cosmetics, as well as hazards associated with contaminants entering the food supply. The Environmental Protection Agency is responsible at the present time for regulating most other chemicals. Regulatory toxicologists also are involved in the establishment of standards for the amount of chemicals permitted in ambient air, in industrial atmospheres, in drinking water, in food, or in feed.

Three other categories of toxicology are designated as *forensic, clinical, and veterinary*:

Forensic toxicology -- a hybrid of analytical chemistry and fundamental toxicological principles. It is primarily concerned with the medicolegal aspects of the harmful effects of chemicals on humans and animals. The expertise of the forensic toxicologist is primarily used to aid in establishing the cause of death and elucidating its mechanisms in a postmortem investigation. These toxicologists usually work for law enforcement agencies and deal with the medical and legal aspects of toxicology.

Clinical toxicology -- designates within the realm of medical science an area of professional emphasis concerned with diseases caused by, or uniquely associated with, toxic substances. Clinical toxicologists may be involved with: teratogenesis and other toxicity-screening

procedures; drug monitoring and drug interactions; drug abuse, addiction, and detoxification; or antidotal treatment of poisoning. Clinical toxicologists may be concerned with the treatment of patients who are poisoned by drugs and other chemicals and the development of new techniques for the diagnosis and treatment of such intoxications. Most clinical toxicologists work in hospitals or poison control centers.

(NOTE: Forensic or clinical toxicologist positions whose duties and responsibilities involve performance of medicolegal autopsies, practice of medicine or direct service to patients, or other work pertaining to food, drugs, cosmetics, and devices and which require a degree of Doctor of Medicine, are excluded from coverage of this series.)

Veterinary toxicology -- concerns the study of the effects of xenobiotics and physical agents in animals and the performance of work that is basic research and not clinically oriented. Veterinary toxicology deals with functional as well as structural alterations in tissues subsequent to exposure to chemicals from any source. The work includes predictive studies (i.e., risk assessment) involving chemical risks. Veterinary toxicologists identify substances that are harmful to animals, as well as substances that may be passed through the food supply and be harmful to humans. Veterinary toxicologists are involved in surveillance of foods for consumption by animals for any type of adulterants, and diagnosis and regulation of adulterants. They monitor toxicological and safety evaluation studies of laboratory animals exposed to chemicals; design experiments; and interpret results. (NOTE: Veterinary toxicologist positions whose work requires a degree of Doctor of Veterinary Medicine, are excluded from coverage of this series.)

It is estimated that currently there are over 30 different specialty areas in toxicology. Some examples of the major specialty areas within the toxicology field include the following:

Behavioral toxicologists -- study subtle changes in behavior for indications of chemically induced toxic effects. The objective of behavioral research is to explore the potential utility of using subtle, but quantifiable, changes in innate behavioral patterns as early indicators of chemically induced toxic effects. Basic research in this type of exploratory program is directed toward assessing the effects of neurotoxic chemicals on pain perception in laboratory animals; and sensory and cognitive as well as motor function tests. Because subtle behavioral changes may precede gross functional deficits, this research can have implications for both toxicological testing and basic research programs.

Biochemical toxicologists -- study changes in cell functions for clues to the biochemical mechanisms which cause them. Major basic research areas are chemical pharmacokinetics and metabolism and analytical chemistry. Some research efforts are directed toward the identification of molecular aberrations of cell function. Detection of such changes leads to research programs intended to elucidate the biochemical mechanisms through which chemicals induce these effects and produce cellular, tissue, or organ damage. Studies of chemical disposition, accompanied by separation and identification of metabolites, are conducted to explain mechanisms of toxic effects detected in long-term toxicity studies.

Environmental toxicologists -- assess the toxic effects of chemicals, such as pesticides on environment. They are concerned with air, water, and soil pollution and assess the hazard of exposure to chemical or physical agents. The environmental toxicology area has as its goal the development of an understanding of the principles which govern the site and severity of damage to biota by environmental agents. The focus is upon processes by which environmental agents affect biological systems and by which biological systems, in turn, influence the action and fate of debilitating agents.

The environmental toxicologist or food toxicologist may be dealing with an unidentified material, its metabolite, or a substance of undefined chemical nature or biological activity naturally occurring in foodstuffs or other sources of environmental exposure.

Genetic toxicologists -- explore chemically induced genetic damage. Many industrial chemicals, food additives, therapeutic drugs, or pesticides are capable of interacting with the genetic material of cells and thus present an increased risk of damage to humans and animals. Chemically induced genetic damage and its relationship to chemical carcinogenesis is well documented. However, the biological and biochemical basis for such chemically induced genetic alterations and the reasons for the observed mutagenic/carcinogenic correlation are not well understood. Research programs seek to clarify biological mechanisms involved in these phenomena, and to foster a clearer assessment of the risks posed to humans and animals by chemical exposure, through the use of so-called "short-term tests." Research programs include both development and improvement of new assays, and the use of these assays in the clarification of mechanisms of chemically induced genetic damage and its relation to chemical carcinogenesis.

Inhalation and respiratory tract toxicologists -- test the adverse biological effects of chemicals in the air as gases, vapors, and aerosols. They also collaborate with other researchers in designing inhalation tests for specific chemicals. Inhalation toxicology, to fulfill the basic research functions for an organization, requires expertise in the generation of test atmospheres of gases, vapors, and aerosols.

Reproductive toxicologists -- study toxic effects on the reproductive process and system. Use tests to identify chemicals that may cause birth defects, fetal toxicity, behavioral changes, infertility, or that may damage reproductive functions.

Neurotoxicologists -- probe into the effects of exposure to toxic substances on human and animal nervous systems. Toxic substances include pesticides, drugs, and other chemicals including those found in the workplace and in consumer products (e.g., food, detergents, and solvents).

Immunological toxicologists -- study the effects of various substances on a special body system. Develop various in vivo and in vitro methods to identify chemicals which cause immunodeficiency or immune suppression, allergies, and hypersensitivity, or which alter host defense mechanisms. Use in vivo tests to identify chemicals which cause toxic effects or alter host response to bacteria, viruses, parasites, and tumor cell challenge. Define the mechanisms of chemically induced immunotoxicity.

REQUIRED KNOWLEDGES

Knowledge and skill requirements for toxicologists include those necessary to:

(1) assess the adverse effects of chemicals and other toxic substances and the probability of their occurrences (e.g., functions required under the Toxic Substances Control Act and similar statutes);

(2) design and evaluate research protocols for the safety evaluation of compounds of poorly known or unknown toxicological characteristics; and/or

(3) engage in research that ultimately leads to the development of new, more precise and reliable methods of evaluating the potential effects of chemicals on humans and animals.

Acquisition of these required knowledges typically results from cross-disciplinary training in several fields of the biological sciences that underlie toxicology. Training in the biological sciences usually is augmented by training in the relevant physical sciences (such as biochemistry, organic chemistry, and physics) and mathematical and statistical sciences.

General toxicology training includes work in methodology (testing of compounds and analytical methods), carcinogenesis-mutagenesis-teratogenesis, industrial toxicants, environmental toxicology, comparative toxicology (the emphasis here might vary from insects to mammals or plants), molecular mechanisms of toxicity, and organ-specific toxicity.

As a multidisciplinary science, toxicology has both basic and applied aspects. Basic sciences and areas of application that contribute to the acquisition of core toxicology knowledges and skills include the following:

Basic Sciences	Areas of Application
Anatomy	Behavioral toxicology
Biochemistry	Chemical dispostion
Biostatistics	Detoxification
Chemistry	Ecotoxicology
Cytology	Inhalation toxicology
Ecology	Mutagenesis
Embryology	Oncology
Epidemiology	Regulatory process
Genetics	Reproduction
Histology	Risk assessment
Immunology	Teratogenesis
Molecular biology	
Pathology	
Pharmacology	
Physiology	
Toxicology	

The field of toxicology is a principal discipline that encompasses many specialty areas, and many toxicological assessments require multidisciplinary approaches, particularly in the area of safety evaluation. An interdisciplinary approach also may be used in other work situations. Scientists trained in other disciplines often work with toxicologists to apply their various professional perspectives to the problem at hand. Biochemists, biologists, ecologists, entomologists, epidemiologists, geneticists, physiologists, pathologists, and veterinarians often comprise a multidisciplinary group engaged in toxicological work. Final hazard assessments which typically are the responsibility of the toxicologist incorporate the scientific judgment of many such disciplines in the biological, physical, environmental, and medical sciences.

MAJOR DUTIES AND FUNCTIONS

The work of the toxicologist embraces a wide range of activities that are concerned with the development and interpretation of data required for risk assessment and safety evaluation of chemicals and physical agents, including actual or potential human and animal health effects and environmental aspects of toxicology. Toxicologists represent varying levels of expertise -- from professional trainees conducting in vivo and in vitro toxicity screens to laboratory supervisors to executives managing large programs of risk assessment.

The scope of toxic substances related activities supported by Federal agencies extends over a wide spectrum of subject matter areas. These include, but are not limited to, the following:

-- Projects investigating human and animal exposures, including different routes of exposure and health effects, and variations in susceptibility to toxic chemicals;

-- Projects on mechanisms of action, disposition and/or pharmacokinetics of toxic chemicals in animals and humans; development, modification, and/or validation of test systems (including animal) for detecting, characterizing or predicting human health effects;

-- Other activities including information systems (e.g., the toxicology public information and reference services that provide technical information for chemical selection, experimental design, and bioassay report preparation); development of more accurate and standardized methods of chemical analysis; chemical characterization of toxic substances; and strategy modeling techniques.

In many Federal regulatory agencies, toxicologists contribute to programs that seek to meet broad social goals. Scientists in this role make hazard analysis decisions and provide for the safe manufacturing, handling, use and disposal of many types of consumer material. In meeting these objectives, toxicologists typically undertake work that defines the biological effects of a chemical (the adverse or beneficial consequences occurring following exposure) and measures potency (how much of a chemical is required to bring about an effect). In most instances, the toxicologist seeks to determine not only the effects of a chemical following relatively short-term, high-level exposure but also tries to determine the long-term, low-level exposure consequences over a lifetime.

Toxicology work often is used as a basis in social judgments related to toxic chemicals, e.g., risk/benefit analyses and other kinds of decision making. Some toxicologists in the Federal services are engaged in agency toxic substances activities including the research roles of various Government organizations. The Federal Government supports a widely varied research effort on toxic substances involving a diversity of research scientists. The areas of greatest activity are in dispersion, control technology, and the mechanisms of action of toxic agents. A substantial amount of research is being performed in aquatic areas, including uptake by edible sea life and in human exposures. Some research is being conducted on the terrestrial side which involves primary food chains, agricultural crops, and animal science. Some agencies participate in bilateral or other international agreements involving toxic substances.

Toxicologists identify and promote scientific principles in the fields of genetic toxicology and carcinogenesis. They develop statements that may serve as a basis for guidelines and regulations in the national or international context, with the object of minimizing or preventing deleterious effects in humans and animals due to the interaction of chemicals with genetic material. For example, toxicologists:

-- prepare critical evaluations of the current body of knowledge that may serve as a basis for establishing priorities for further research or possible regulatory action;

-- identify substances and situations that may entail significant "genotoxic" hazard to humans and animals.

From an environmental research standpoint, toxicologists do not deal exclusively with the effects of xenobiotics on humans. A substantial concern involves the effects of xenobiotics on fish and wildlife and their food organisms as well as on domestic animals. This concern also extends to consumption of these organisms by humans or animals as an important indirect means by which pesticides and other toxic organics and inorganics enter the body and thereby exert their toxic effects. 27, 7/87, TS-81

From the standpoint of food and drugs, toxicologists responsible for participating in this aspect of regulatory decision-making concerns are involved in examination of direct and indirect food additives, food, drug and cosmetic color additives, and cosmetic formulation and ingredients, and drugs for food producing animals.

The responsibilities of toxicologists in national health programs grow out of their various research programs involved in the search for causes, means for prevention, and cure of a wide variety of diseases. Thus, the national health programs' use of toxicologists in basic and applied research is somewhat different from the focus of those engaged in regulatory decision making.

Experimental toxicologists perform safety evaluations to provide data required by the regulatory agencies upon which societal decisions can be made as to whether or not the general population should be exposed to a certain material.

Individuals who add to the fundamental knowledge base of the science of toxicology by furthering understanding of mechanisms of action and by developing new testing methodologies, thereby produce new knowledge about the effects of chemicals on organisms. This new knowledge then allows safety evaluation procedures to become more precise and more capable of predicting the true hazard in the real world.

Research toxicologists, particularly in regulatory agencies, recommend actions or information needs on chemical safety assessment submissions. These procedures go beyond "checklisting" as the *modus operandi* -- rather, sound scientific judgment is utilized in implementing Federal Government regulations.

Another aspect of toxicology is concerned with identifying, predicting, understanding, assessing, and ameliorating the effects of toxic factors and compounds in the physical environment on

human and animal health. To accomplish this, the scientist must possess the knowledge necessary to identify those chemicals or physical agents which are most likely to exert adverse effects on human and animal health to understand how they damage health or cause disease. This type of research focuses on the following:

-- metabolic studies (how the body processes the chemicals);

-- mechanisms of action studies (how normal body processes are disturbed by the presence of the chemical and/or its metabolites);

-- test development efforts to find new methods to better predict the potential hazard to humans or animals of exposure to environmental chemicals or physical agents;

-- epidemiological methods identifying various potential health hazards now in the environment.

The results of this type of research are important to Federal regulatory agencies, since a new testing methodology or new information about a regulated chemical often shows the need for a modified regulatory posture.

Toxicologists in the Federal service participate in a broad spectrum of supportive activities in other research areas such as:

-- evaluation of toxic hazards to nontarget biota from the use of pesticides, herbicides, fungicides, rodenticides, and other toxic chemicals for insect and disease control and silvicultural purposes;

-- determination of the extent, magnitude, and consequences of nonpoint source pollution through chemicals used in forest and range management;

-- agents encountered in aviation activities which may threaten the health and well-being of aviation personnel or jeopardize safety in flight;

-- aeronautical, aerospace, and missile systems health hazards (including new weapons and space systems);

-- radiation hazards.

TYPES OF ACTIVITIES

Toxicologists involved with activities as they relate to studies concerning the actions of chemicals on biologic mechanisms may conduct such studies at different levels within an organization, depending on the respective organization's direction of interest. These types of studies primarily are designed to: 1) evaluate the general overall effects of compounds on experimental animals; and/or 2) evaluate in detail specific types of toxicity. With the exception of acute toxicity, most tests are conducted for the purpose of determining the nature of any toxicity that can be produced by repeated dosing of animals over an extended period of time and for estimating the degree of safety of a material for humans and animals. The more commonly used tests are defined as follows:

Acute toxicity tests: the single test that is conducted on essentially all chemicals that are of any biologic interest; the compound of interest is administered through the oral, inhalation, or dermal route on one occasion. The purpose of the test is to determine the symptomatology consequent to administration of the compound and to determine the order of lethality of the compound.

Prolonged toxicity tests: the general evaluation and characterization of the effects of compounds when they are administered repeatedly. These tests involve the application of analytical techniques for determining effects on blood chemistry and blood cells, urine chemistry, organ tissues, specific organ functions, central nervous/autonomic nervous system, and the immune system. Prolonged tests may, and chronic tests will, include microscopic examination of body tissues.

Chronic toxicity tests: conducted primarily to determine the toxicity or level of toxicity in addition to the absence of toxicity when the doses involved represent some practical level, and also, the carcinogenic potential of a compound.

Potentiation tests: designed to provide information regarding the summation of biologic effects when two or more agents with similar action are simultaneously administered, or antagonisms that may occur when agents are or are not given simultaneously.

Teratologic tests: teratogenic studies of the courses, mechanisms, and manifestations of deviant development of a structural and functional nature, induced by chemicals that produce embryotoxic effects.

Reproduction tests: studies designed for evaluation of chemical-induced effects on fertility and reproduction including multigeneration tests that provide for accumulation of effects of the agent to the point where toxicity is manifested.

Mutagenesis tests: analysis of the induction of those alterations in the information content (DNA) of an organism or cell that are not due to the normal process of recombination. (The problem of human and animal contact with increasing numbers of substances in the environment, including drugs, food additives, and pollutants, has led to increased interest in the development of methods for detecting possible mutagenic effects of these substances.)

Carcinogenicity tests: evaluations of chemicals (carcinogenic agents) that are capable of producing any type of tumor. Most tests for carcinogenicity are performed on food additives or pesticides.

Skin and eye tests: study of chemical injury resulting from a variety of routes of exposure including absorption through the skin, also, substances that come into contact with the eyes. Information is obtained on the relative ability of substances to produce injury in the course of customary intended use and in the course of reasonably anticipated misuse. Chemical entities tested included those in the form of soaps, detergents, emulsifiers, cosmetics, solvents, and dyes. Phototoxicity is an extension of this field.

Behavior tests: tests for toxicity designed to demonstrate effects on behavior of animals; the quantitative evaluation of activity and specifically locomotor types of activity of experimental animals. Such tests in toxicology typically involve indepth studies on heavy metals (e.g., mercury and lead salts) and nervous system toxicants (e.g., cyanide, organophosphates, and DDT).

Toxicologists also are engaged in activities as they relate to: (a) basic research into mechanisms of toxicity, i.e., understanding why the tests show what they show; (b) the development of new, more expeditious or more accurate testing methods; and (c) the investigation of outbreaks of human or animal disease to discover toxic chemical causes, if such exist.

BASIC QUALIFICATION REQUIREMENTS

Work in toxicology requires indepth professional education and experience in toxicology and knowledge of:

(1) the use or interpretation of a full range of techniques, procedures, and methods applied to assess the deleterious action of chemical compounds and substances on biological systems;

(2) the methods used to detect and evaluate the nature of chemical-induced changes in function and structure; and 31, 7/87, TS-81

(3) the significance of certain effects on living cells.

Also required are knowledges of the principles and concepts utilized in toxicological relationships sufficient to enable the toxicologist to:

(1) appropriately recognize and quantify relative hazards of various types, levels, and durations of use or exposure; and

(2) develop the perspectives needed to make reasonable predictions concerning their impact on human and other living populations including future generations and the environment in which they live.

The required knowledge and experience typically are of such an advanced nature that most positions require a Ph.D. in toxicology or equivalent education and training. However, some developmental or limited assignment positions may be filled by candidates with less formal education and experience.

TITLES AND SPECIALIZATIONS

The basic title for all positions in this series is "Toxicologist." The title "Supervisory Toxicologist" is to be used for those positions that involve supervisory duties and responsibilities that meet or exceed the criteria for evaluation as a supervisor in the General Schedule Supervisory Guide.

Toxicologists may specialize in a variety of ways, such as by a particular source or nature of the substance (e.g., environmental, pollution, residues, drugs, devices, pesticides, food, or cosmetics); by particular groups of organisms (e.g., human, fish, wildlife); or by function or place of work (e.g., industrial, clinical, forensic, regulatory, or research). Additionally, within the specialties themselves, subspecialties may emerge (e.g., genetic toxicology, reproductive toxicology, immunotoxicology, oncogenic toxicology, and neuro-behavioral toxicology).

Many toxicologist positions involve a high degree of specialization in unique work situations, each with a somewhat distinct set of knowledge, skill, and ability requirements. However, there are basic knowledges and skills that are transferable from work in one specialty area to work in another.

Separate identification of a large number of specialties and subspecialties is considered impractical, tending to complicate classification practice and encourage the development of artificial barriers to movement between specializations. Therefore, subject matter specializations for this area of work have not been established. The required specialized knowledge should be considered, as necessary, in selective placement and other personnel actions.-81

EVALUATION NOTES

This series-coverage standard does not include grade-level criteria. Research positions should be evaluated by reference to the Research Grade Evaluation Guide. Positions primarily concerned with evaluating and recommending approval of toxicological research grants and contracts should be evaluated by reference to the Research Grants Grade Evaluation Guide. Part II of the General Schedule Supervisory Guide should be used to evaluate supervisory positions. Other types of toxicologist positions should be evaluated consistently with published standards by cross series comparison. Among the published standards that might be used as cross references are those for the Microbiology Series, GS-0403, the Entomology Series, GS-0414, and the Chemistry Series, GS-1320.