## Properties and Units for Transfusion Medicine and Immunohematology

***K. Varming, U. Forsum, I. Bruunshuus, and H. Olesen***

*Pure and Applied Chemistry*
Vol. 75, No. 10, pp. 1477–1600 (2003)

Basic research in biology and medicine and innovations in laboratory methodology have increased greatly the range of properties available to medical staff to help them in decisions involving the diagnosis and prevention of disease and the treatment of patients. The plethora is now such that the individual doctor may have insight into or understanding of only a few of the properties offered to him from the various clinical laboratory specialties. Further, recent developments tend to blur the boundaries between the various disciplines of clinical laboratory sciences; the same properties are being reported differently in different disciplines.

The terminology used by one laboratory specialty may vary even within the specialty, and even be incomprehensible to another area. This is a minor inconvenience to the laboratory specialties, each being concerned essentially with its own area of activity. However, for the user, this is unsatisfactory and it may even hinder treatment of the patient.

To alleviate this problem, coding schemes combining a definition of a specific property with a particular code have been developed in the various specialties of the domain of clinical laboratory medicine. This allows the requester of analyses, and the producer and the receiver of the results, to express the concept as is most convenient locally.

Often the format of presentation is restricted by the number of signs allocated for this purpose in the database. For example, the definition "Blood (capillary Blood)-Glucose; substance concentration = ? mmol/l" is coded by NPU10113. A request for "Blood sugar" identified by the code NPU10113, may be reported back as "NPU10113: B(cB)-Glucose; subst.c. = 6,5 mmol/l" or "NPU10113: 6,5", and be registered in the patient file of a general practitioner as "NPU10113: Gluc. 6.5". The concept identified by "Erythrocytes(Blood)-Erythrocyte antigen; taxon(AB0;RhD; procedure) = ?" is coded by NPU01945. A request for "NPU01945 blood-typing" may elicit the report "NPU01945: Ercs(B)-Erythrocyte antigen; taxon(AB0; RhD; proc.) = A; RhD negative", and be registered in the patient file as "NPU01945: A; RhD negative".

Each of the clinical laboratory specialties adapts well to the general structure for presentation of properties and the adhering kinds-of-property. However, often a particular kind-of-property, not used in any other specialty, is required; for transfusion medicine and immunohaematology the kind-of-property "compatibility" is unique.

The coding scheme for clinical laboratories is operating in Denmark and in Sweden. It has shown both practicability and usefulness; it has eliminated a number of ambiguous presentation formats and it adapts well to electronic patient records.

This document is part of an ongoing effort to standardize transmission of laboratory data across cultural and linguistic domains, without attempting to standardize the routine language used by clinicians and laboratory practitioners. It comprises a general introduction and an alphabetic list of properties. The list is based on the syntax for properties recommended by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and IUPAC. The nomenclature is primarily from the Working Party on Terminology of the International Society of Blood Transfusion.

A manuscript on molecular biology has been finalized and is pending acceptance by IUPAC and IFCC. If it is accepted, the coding scheme covers clinical chemistry, with the exception of chromosome studies and the molecular biology of mitochondria. The scheme comprises some 35 000 entries, or sets of definition and code.

**www.iupac.org/publications/pac/2003/7510/7510x1477.html**

## Implications of Endocrine Active Substances for Humans and Wildlife

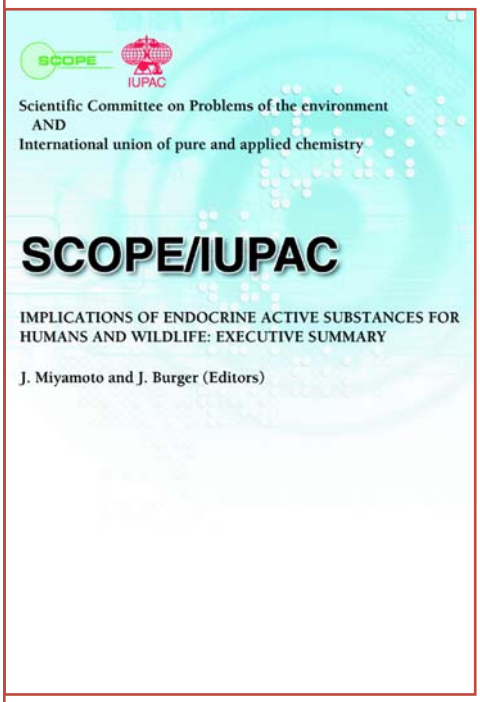
***A special topic issue edited by J. Miyamoto and J. Burger***

*Pure and Applied Chemistry*
Vol. 75, Nos. 11–12, pp. 1617–2615 (2003)

Understanding the scientific issues surrounding endocrine-active substances (EASs) is an international priority. Endocrine disruptors affect not only humans, but also other living organisms. They affect not only our generation, but also future generations. Though the adverse effects of endocrine disruptions (EDs) were noted as far back as 30 years ago, inten-

sive studies of endocrine disruptors have only begun in the last decade. The present SCOPE/IUPAC project on endocrine active substances is the only project looking at these potentially harmful substances on a world-wide basis, with emphasis on the specific situation in each region.

An endocrine disruptor may be defined as ". . . an exogenous substance that causes adverse health effects in an intact organism, or its progeny, secondary to changes in endocrine function." Simplified models exist that can be used to assess hazards and risks, but should be a priority to adjust these models as new insights on larger scales impact the accuracy and relevance of the basic methodologies.




In 1998, a committee involving representatives from IUPAC, IUTOX (International Union of Toxicology), and IUPHAR (International Union of Pharmocology) made recommendations in the "White Book" on endocrine disruptors. One recommendation was to establish a better understanding of the impact of particular chemicals on the environment, as well as a need for better screening, testing, and risk-assessment methods.

In the project Environmental Implications of Endocrine Active Substances: Present State-of-the-Art and Future Research needs, there were four focus areas: nuclear receptor mechanisms, fate and metabolism of EASs, effects in rodents and humans, and effects in wildlife species.

Recent studies have indicated that exposure of humans to EASs potentially can have many effects, ranging from abnormal maturation to cancer. However, it is difficult to establish whether these conditions are caused by, related to, or in actuality, completely independent of EASs. Though several tests are designed to detect ED disease conditions, as some diseases are evident only after chronic exposure or long latency, it is necessary to revise testing techniques as scientists become more knowledgeable of cause-effect relationships. During the last decade, it is notable that there have been no conclusive findings of human disease caused by low-level environmental exposures to EASs.

In addition to humans, over 200 wildlife species either are known, or are suspected to have been, affected by EASs. Though most examples of ED in wildlife have been reported from Europe, North America, Japan, and Australasia, it is possible that this reflects the current global distribution of research efforts. Highly contaminated areas with significant human populations typically show the most significant effects on wildlife, but even lower levels of exposures to particular substances can occur in less-developed areas. The greatest exposure has been shown in aquatic life, but again, it is possible that this is due to the concentration of current investigations on this area.

The project culminated in a symposium held 17–21 November 2002 in Yokohama, Japan. Scientists, managers, and public policy-makers presented papers on human effects, wildlife effects, exposure assessment, and testing for EASs and ED effects. There were six workshops dealing with the effectiveness of QSAR toxicogenomics, integrated monitoring systems, rapid assays, precautionary principle/weight of evidence approaches, and risk management options for endocrine disruptors. Overall, 408 scientists gathered from 31 countries, giving 84 talks and contributing an additional 84 posters. The papers presented form the basis of this special issue of *Pure and Applied Chemistry* (Vol **75**, Nos 11/12, 2003). The issue also includes an executive summary edited by J. Miyamoto and J. Burger.

At the meeting, a range of needs was identified that applies to all aspects of the study of ED and EASs. The field of ED is rich in unexpected observations-consistent with evolving methodologies and the state of our understanding of the underlying biology of the endocrine systems. However, the science will be aided by a renewed commitment of researchers to

follow the scientific method.

Assessing the exposure of living organisms means uncovering the sources, transport, and fate of EASs in environmental media through organism contact, bioavailability and absorption, and distribution to target tissues or receptors. The substantial literature on chemical exposure assessment, in general, may be applied to EASs. Long-term cryobanking of human and wildlife specimens will allow for retrospective evaluation when new priorities arise. By sampling indicator species and measuring biomarkers, researchers should have advance warning of problems. Sustained programs for monitoring EASs—that emphasize substances of high-potency and high-exposure potential that may pose a real risk for humans or the environment—require sustained investment and public support.

It is important to note that *in vitro* tests, alone, cannot be used to define ED activity, as no endocrine system is being monitored. To uncover whether an EAS will show ED activities, it is necessary to use assays based on a whole organism. Uncertainty regarding whether some EASs may possess the ability to induce effects at doses below those considered safe using current testing methodologies should be evaluated urgently and resolved.

In all areas of study, there may be sensitive subgroups of exposed individuals that may show much greater responses than the majority. This could lead to a loss of information if this potential is not recognized. It is therefore important to obtain better statistical methods for detecting such effects, which may be obscured by population-based, parametric statistical analysis alone.

Methodologies need to be developed to improve quantitation and understanding of both the certainties and the uncertainties associated with extrapolating experimental animal data, derived from multiple studies using different endpoints, to effects expected at ambient levels of environmental exposure.

Consensus on definitions and applications of the *precautionary principle* and the *weight of evidence approach* should be sought. At present, these two concepts compete for attention and are subject to a range of definitions. The precautionary principle also allows action when the probability of an adverse effect may be low, but consequences are considered large and/or irreversible, and the cost of preventive action is acceptable to society. Some believe that this represents action when a hazard should exist, but is not necessarily evidenced; others believe it to indicate the evidence is overwhelming, but ultimate proof does not exist. Meanwhile, the weight of evidence approach is regarded by some as a numerical averaging of positive and negative data sets, while others regard it as an expert integration of all available data (which may include the explicit consideration of clear but isolated findings).

Because screening assays provide qualitatively different information than definitive tests, the results from these dissimilar assays should be used in a manner that is consistent with the scientific basis and purpose of each. To advance our understanding of the relative merits and disadvantages of these different approaches to risk management, it is essential to examine some examples of actions that have been taken on EASs, compare the different outcomes, and decide which are preferable.

Scientific gaps and uncertainties remain large, and will continue for some time. However, the in-depth, comprehensive, authoritative review by SCOPE and IUPAC of EASs and their environmental and health effects will facilitate risk assessment and assist governmental and intergovernmental authorities, industry, and the wider public in framing policies to address these issues.

What is the future of research in EASs and EDs? While past and present research and techniques are useful, the methods and approaches must be continuously modified and perfected to incorporate new discoveries. We have learned that the global effects attributed to EASs are not as all pervading or fearsome as some have asserted, nor as trivial as others would wish. The beauty of science is that "more research is always needed," and our quest for understanding the world around us is boundless. However, the most important question regarding ED is: What are the significant effects of EASs in terms of health, well-being, and population stability of humans and wildlife? As humans continue to evolve, so will the study of endocrine-active substances.

**www.iupac.org/publications/pac/2003/7511/**
**www.iupac.org/news/archives/2003/pr-031030.html**