Green Analytical Chemistry

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Foreword

The pursuit of Green Analytical Chemistry is an emerging field of endeavor that has already shown great achievements and even greater promise and potential for the future. As we consider that the word *analysis* means: "the resolution of anything complex into simple elements," it reminds us that to affect any complex system we must first understand it. Essential to our understanding is analysis. This is particularly important in the area of Green Chemistry.

Green Chemistry is centered on the concept of design. The definition of *Green Chemistry* itself is: "the *design* of chemical products and processes that reduce or eliminate the use and generation of chemical products and processes that reduce or eliminate the use and generation of hazardous substances." In order to design something you have to deeply understand it. You cannot design something by accident. If it were an accident, it wasn't design. Analysis is essential therefore to achieving the depth of understanding needed for design; design of products, processes, and systems.

Green Analytical Chemistry not only informs design by providing insight, it is currently reinventing the field of chemical analysis itself. It was not so long ago that there were studies done to identify some of the major significant waste generators in various industrial sectors. Surprisingly on the list were the environmental analytical laboratories. The same laboratories that were so essential in monitoring, measuring, and characterizing environmental problems, were themselves generating environmental problems. This was largely due to the quantity of solvents that were used at the time of the studies. Upon seeing these studies, I posited the mostly humorous, Anastas Environmental Analysis Principle (with apologies to Heisenberg) – "One cannot measure an environmental problem without causing another environmental problem." The great potential of Green Analytical Chemistry is to continue to make this "principle" antiquated and increasingly false.

One of the Twelve Principles of Green Chemistry deals exclusively with analytical chemistry in pursuit of real-time, in-process, in-field, non-destructive, non-materially or energy-intensive analysis. This book provides important insights into the various methodologies and techniques that are at the cutting edge of this rapidly growing field. The contributors to this volume are to be commended for their vision and insight. Readers of this volume, especially students, will find fertile research areas to grow new projects and technologies.

There is a story of a sign that supposedly hung in Einstein's office that read, "Not everything that can be counted counts, and not everything that counts can be counted." The astounding success of chemical analysis over the past century and even more so in recent decades, has made it clear that our ability to analyze needs to be coupled with our ability to characterize. Our ability to generate data is increasing at an astounding rate. Our ability to transform the data into information must strive to keep pace. The Green Analytical Chemistry challenge is to couple these abilities with the perspective that the ultimate goal is to generate knowledge and perhaps even wisdom. Only in this way will we have the ability to move the planet and civilization toward a sustainable trajectory. In the assessment of analytical instruments, the compass is more important than the speedometer. While it is often good to go faster and faster, it is more important to know that you are heading in the right direction. This book is an important step in the right direction.

Paul T. Anastas
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Preface

The principles of Green Chemistry are reaching into all the chemical disciplines. There is increasing demand for chemical analysis and the development of analytical chemistry continues at a steady rate. Every new discovery in chemistry, physics, molecular biology and material science has an application in analytical chemistry as well.

The use of toxic compounds and solvents in chemical analysis is an extremely pressing issue that makes Green Analytical Chemistry an emerging hot topic in industrial and governmental laboratories as well as in academia.

However, the relationship between Green Chemistry and Analytical Chemistry is especially close because analytical chemistry provides the means of evaluating and justifying Green Chemistry and is an efficient tool for determining the "greenness" of a chemical product or technology.

On the other hand, methods of chemical analysis cannot avoid the use of solvents, reagents and energy, and thus generate waste. The application of a Green Chemistry perspective in the assessment of analytical methods should be a natural development in chemistry and should coincide with its basic policy. Being green is a "must" in contemporary chemical analysis, *i.e.* the true cost of resources and generation of waste must be included in the design of every new method and in every comparison of procedures. It can be said that the goal of Green Analytical Chemistry is to employ analytical procedures that generate less hazardous waste, are safer to use and more benign to the environment.

This book is a modest attempt to portray the changing situation in analytical chemistry with regard to adopting the principles of Green

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Chemistry. There are many other textbooks on different aspects of Green Chemistry, but none on Green Analytical Chemistry. We hope to fill this gap to some extent. The rationale for writing this book on Green Chemistry is to describe the current application of green principles in analytical chemistry and to comment on what more needs to be done. The main emphasis in analytical chemistry is on the metrological quality of the data, and only recently has attention been directed toward the environmental aspects of the way the data are obtained. In view of the theoretical as well as the practical importance of this subject, we urge the scientific community to exert itself in this respect.

The first two chapters are devoted to the general aspects of Green Chemistry and trends in analytical chemistry. An overview is provided of existing techniques for sample preparation and instrumental analysis in the context of solvent usage and safer chemicals. The next chapters review the current knowledge and efforts in this area, and cover diverse fields of instrumental analytical chemistry, such as separation science, optical and mass spectrometry, and analytical electrochemistry, that could guide others to new ideas and discoveries. The book endorses some prospective methods such as capillary electrophoresis and chemometrics that have been somewhat neglected in the literature on Green Chemistry. Microfluidic technologies have enabled the miniaturisation of established analytical techniques and enhanced performance. The expression "small is beautiful" is more valid in Green Analytical Chemistry than in many other situations. Micronisation can also be exploited to develop completely new approaches to chemical and biological processing.

The book describes efforts to make analytical chemistry greener: the application of Green Chemistry ideas and concepts in chemical analysis, an evaluation of the performance of current analytical methodologies from the perspective of Green Chemistry, and a discussion of the concept of green profiles of methods. We must emphasise that every step toward greening a particular method must respect the main analytical parameters such as selectivity, sensitivity, reliability, analysis time and cost.

This book has been written from an academic point of view; it is meant for senior scientists as well as novices who are just entering the field. The prospective audience for this book is likely to be managers of analytical research laboratories, but the book will also be of interest to teachers of analytical chemistry and even to green politicians.

We obtained most of the information for the book from the publications of scientists in this field. However, we did not attempt to provide a complete review of the literature on this topic. We tried to identify the general trends and the most promising applications that would profit from more attention for further development. There were also time constraints that required us to finish the work by mid-2009. We take responsibility for the choices made in selecting the topics and would be grateful for readers‘ comments on errors, oversights and other useful data on the systems discussed.

Our sincere thanks are devoted to Dolores Talpt Lindsay for her fruitful cooperation and serious efforts to improve our language and Jekaterina Mazina for her help with the illustrations. We are also grateful to the Tallinn University of Technology for supporting the preparation of this book.

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illnesses and improve health, for pure water, and a host of other human activities.

For this reason, energy and sustainable chemistry are key themes in current discussions about the future. Chemicals are present in all spheres of human life. Among other things, they are used as pharmaceuticals, pesticides, detergents, fertilizers, dyes, paints, preservatives and food additives. The first and most influential description of the dangers related to chemicals in the environment is found in Rachel Carson's *Silent Spring*, published in 1962.[1]

Synthetic chemicals end up in the environment in many different ways. The chemical industry is a point source of emissions which create changes around that point. In everyday life the constituents and ingredients of consumer or household products and other open applications emit chemicals into the environment *via* non-point sources. Chemicals and their compositions do degrade and break down into water, carbon dioxide and inorganic salts, but very often the degradation is incomplete. Unknown transformation products can result from such biological and chemical processes as hydrolysis, redox reactions or photolysis. These unknown chemical entities remain in the environment and can be toxic to humans and environmental organisms. The latter situation is more serious as there is usually much less knowledge about the longevity and effects on the environment of the final transformation products than there is about the parent compounds. Even if there is some degree of degradation, the parent compounds will nevertheless remain at constant levels in the environment if the input rate is higher than their rate of degradation or mineralization. This situation has to do with the persistency of chemicals. Persistency is one of the most important criteria in the environmental assessment of chemicals.

Polychlorinated biphenyls (PCBs) are a classic example of persistent pollutants. PCBs were synthesized for the first time in 1877, and as early as 1899 severe health problems (chloracne) associated with the handling of PCBs were reported. Since then, the poisoning of rice oil by these compounds and their neurotoxic effects and carcinogenicity have been described in detail. Despite this knowledge, it was not until 1999 that PCBs were completely banned within the EU – 100 years after the first reports of their severe toxicity. This example clearly demonstrates that it is not only the time lag of the impact of the chemicals on environmental processes, but also the time lag of economic and political systems which has a significant effect.

In 1995, the Governing Council of the United Nations Environment Programme (UNEP) called for global action to assess the effects of POPs (persistent organic pollutants). The twelve worst offenders are known as the "dirty dozen" and include eight organo-chlorine pesticides: aldrin, chlordane, DDT, dieldrin, endrin, heptachlor, mirex and toxaphene; two industrial chemicals: hexachlorobenzene (HCB) and the polychlorinated biphenyl (PCB) group; and two groups of industrial by-products: dioxins and furans. It became clear that these POPs were deadly and that urgent global action was needed. The result was the Stockholm Convention on Persistent Organic Pollutants in May 2001.[2] The Convention outlaws the dirty dozen and also establishes a system to track additional substances that can be classified as POPs, to prevent the development of new problem chemicals.

According to the Stockholm convention, a half-life of more than 50 days in water is set as a criterion for POPs. Recent research has demonstrated that chemicals which are less persistent and have a higher polarity than PCBs are distributed globally as well, and can also accumulate in humans.

An example of pollutants with a much shorter history are the inert organohalogen compounds, known as freons. They were initially developed in the early 20th century as an alternative to the toxic gases that were used as refrigerants, such as ammonia, chloromethane and sulfur dioxide. These compounds, which contain only chlorine, fluorine, and carbon, are called chlorofluorocarbons (CFCs). Each freon product is designated by a number. For instance, Freon-11 is trichlorofluoromethane and Freon-12 is dichlorodifluoromethane. The most common is Freon-113, trichlorotrifluoroethane, used as a cleaning agent.

In the 1970s, scientific evidence showed that human-produced chemicals are responsible for observed depletions of the ozone layer. In 1978, the United States, Canada and Norway enacted bans on aerosol sprays containing CFC that are thought to damage the ozone layer. After the discovery of the Antarctic ozone hole in 1985, CFC production was sharply limited as of 1987 and was phased out completely by 1996 according to an international treaty. The Montreal Protocol on Substances that Deplete the Ozone Layer classifies Freon-11 and Freon-12 as Annex A substances, and bans their production and consumption.[3] It has now been confirmed that the upper atmosphere ozone depletion rate has slowed significantly during the past decade.

The interim replacements for CFCs are hydrochlorofluorocarbons (HCFCs), which contain chlorine that depletes stratospheric ozone, but to a much lesser extent than CFCs. Ultimately, hydrofluorocarbons (HFCs) will replace HCFCs with essentially no ozone destruction, although all three groups of halocarbons are powerful greenhouse gases.

The Montreal Protocol on Substances That Deplete the Ozone Layer is a landmark international agreement designed to protect the stratospheric ozone layer. The treaty was originally signed in 1987 and substantially amended in 1990 and 1992. The Montreal Protocol stipulates that the production and consumption of compounds that deplete ozone in the stratosphere – chlorofluorocarbons (CFCs), halons, carbon tetrachloride and methyl chloroform – are to be phased out by 2000 (2005 for methyl chloroform).

Chemistry, and the application of chemical technology, can be practised and useful materials synthesised in many ways, some of which are safer for the environment and human health than others. Safety for humans and the environment, as well as the economical use of resources, must be of utmost consideration in the development of new chemical processes. In other words, the true cost of resources and waste must be included in every calculation and comparison. The mind-set in chemistry must be changed from waste treatment to the prevention of waste generation.

New environmental regulations, and a growing social consciousness with regard to the protection of nature, have nudged the chemical sciences and industry toward a new framework in which pollution prevention is the central consideration. This fact presents an enormous technological and scientific challenge that requires the development of innovative products and tools to minimize the impact on the environment. Nevertheless, the same standards of quality and efficiency need to be retained in order to continue scientific advancement within a sustainable framework.

Concerned individuals have raised these questions and citizens are becoming aware of the critical situation. This is also true of chemical scientists and engineers and the chemical industry where a new wind is blowing. A comprehensive and accurate understanding of what constitutes the sustainable development of human civilization is required, taking into account the ecological, economic and social dimensions. This is simple in principle but much more difficult in practice.

In the long term, chemicals end up in the environment. Therefore, an important requirement is to focus not only on the optimization of the chemical synthesis of a molecule and its use, but also to take into account the molecules themselves and their effect on the environment. To quote Anastas and Warner in *Green Chemistry: Theory and Practice*: "Chemical products should be designed so that at the end of their function they do not persist in the environment and do break down into innocuous products".[4] Designing chemicals to meet both the requirements of their application and environmental considerations, throughout their life cycle, is ambitious and quite new. It must, however, become an essential part of the core of chemistry and pharmacy.

Agenda 21, Chapter 35 of *Science for Sustainable Development*,^{5} focuses on the role and the use of the sciences in supporting the prudent management of the environment and development for the daily survival and future development of humanity. "The sciences should continue to play an increasing role in providing for an improvement in the efficiency of resource utilization and in finding new development practices, resources and alternatives. There is a need for the sciences to constantly reassess and promote less intensive trends in resource utilization, including less intensive utilization of energy in industry, agriculture and transportation. Thus, the sciences are increasingly being understood as an essential component in the search for feasible pathways towards sustainable development".

Scientists must develop their basic and applied research topics in accordance with the sustainable development of society. This also applies to chemistry and chemical research topics. Indeed, chemistry – expressed as the courage and curiosity to discover and formulate new materials and compounds to improve human life – plays the most important role in this process. However, chemistry is changing very slowly. Obviously, chemical companies are accustomed to petrochemicals and are reluctant to use alternative renewable feedstocks which may not be well suited to the usual petrochemical processing.

A general process scheme is presented in Figure 1.1 which illustrates the complexity and importance of factors other than the product outcome.

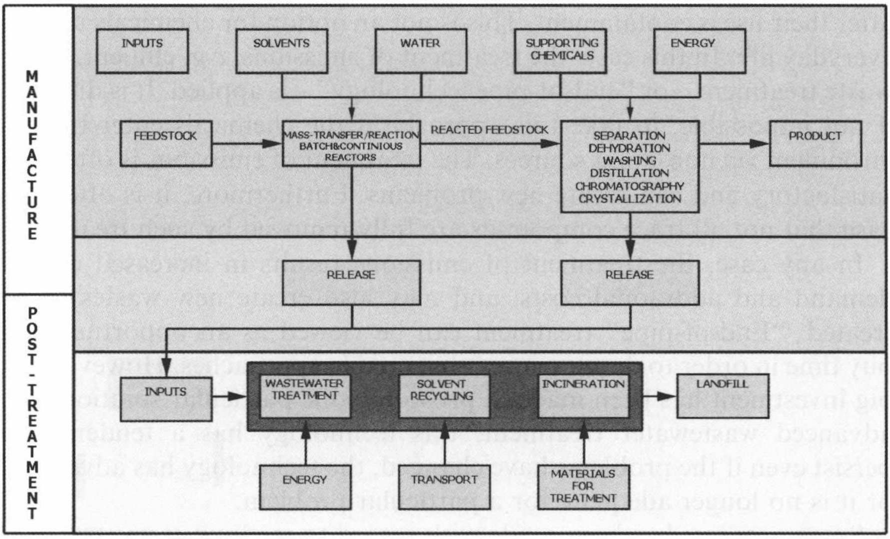

Figure 1.1 General process scheme.

The following describes a pharmaceutical industry manufacturing process based on this scheme. The normal manufacturing yield from a single stage ranges between 35 and 95%, with an average yield of 86% The typical primary manufacturing process involves six stages with an overall yield of 30–40%. Overall yield does not capture the use of reagents, solvents and catalysts. If these are included, the average total materials use is 16 kg/kg of stage product (intermediate). Even with a 100% yield at each stage, a 16 kg/kg ratio of materials use would result in an overall Mass Productivity of about 1%.[6]

These figures demonstrate that a large amount of the materials are not part of the product and could possibly end up in the environment as a result of the process. Reducing the release of these chemicals into the environment has become a crucial issue.

There are at least three options for decreasing the input of chemicals into the environment:

- the technical approach: advanced treatment (short- to medium-term);
- the education and training of users, *e.g.* retailers and consumers (medium-term);
- the substitution of critical compounds with benign ones (long-term).

The traditional short- to medium-term approach for the prevention and reduction of the input of chemicals into the environment during and after their use is containment. This is not an option for chemicals used in everyday life. In this case, the treatment of emissions, *e.g.* effluent, air or waste treatment – or "end-of-pipe technology" – is applied. It is difficult, if not impossible, to take this approach if the chemicals enter the environment *via* non-point sources. The treatment of emissions is often not satisfactory and can create new problems. Furthermore, it is often the case that not all trace compounds are fully removed by such treatment.

In any case, the treatment of emissions results in increased energy demand and additional costs, and may also create new wastes to be treated. "End-of-pipe" treatment can be viewed as an opportunity to buy time in order to develop more sustainable approaches. However, if a big investment has been made in providing one particular solution, *e.g.* advanced wastewater treatment, this technology has a tendency to persist even if the problems have changed, the technology has advanced, or it is no longer adequate for a particular problem.

Some progress has been made with regard to medium-term strategies and containment at source. Responsible care and product stewardship have been created and implemented within a number of industries, which has contributed to the reduction of emissions. In the case of chemicals used in open systems, this approach has its limitations and is not always very efficient.

The third and long-term approach is the objective of Green Chemistry – to make chemistry itself more sustainable, and the key to sustainability is the design of chemicals and pharmaceuticals which are not harmful to the environment. One approach is to design chemicals in such a way that they are readily degradable after their use. This means that the functionality of a chemical consists of more than just the properties required for successful applications. Functionality in a broader and sustainable sense would also include the rapid and complete degradability of a molecule after its use, for example in traditional sewage treatment. According to this assumption, when new chemical entities are created, it is necessary to take into account both the properties required for successful applications as well as what happens to them afterwards.

Compounds with few or no side effects or low toxicity can be called inherently safe. Such chemicals need little or no safety measures or special knowledge on the part of the user or applicant. A simpler expression of this concept is that chemicals should have the lowest possible impact on humans handling and ingesting them and also on the environment. If the environment is exposed to such compounds, no effects have to be considered. This calls for a different understanding of the functionality of a chemical: its manufacturing and use, as well as its fate after use. Such chemicals are benign by design. A life cycle assessment and optimization is conducted according to the specific conditions present at the different stages of a chemical before its synthesis and introduction into the market.

These steps include:

- raw materials
- synthesis
- production
- use
- fate after use

Such an approach requires the chemist performing the synthesis to have a different mind-set. He has to take an interdisciplinary approach and consider the world outside his laboratory. He is not only a craftsman who assembles molecules, but also an architect who designs them. This entails accounting for not only the functionalities of a molecule that are necessary for its application, but also for those