Clean laboratories: Past, present and future

J R Moody

Chemical Science and Technology Laboratory, National Institute for Standards and Technology, Gaithersberg MD USA 20899.

Abstract

Clean chemistry laboratories have become rather ubiquitous for the ultra-trace analysis of elements, especially among those laboratories that work in the area of isotope geochemistry. The need for the control of analytical blanks has almost always been appreciated, but became the primary concern of analysts as new measurement technology opened the door to elemental measurements on amounts of substance equal to a nanogram or less. Since common laboratory environments expose samples to a contaminant deposition of up to one microgram in a 24 hour period, cleaner environments were recognized as necessary. In the 1960s, a number of laboratories applied clean air technology from the space and electronics industries to the chemical laboratory.

The results from these pioneering efforts and the need to accurately measure elemental and isotopic compositions on the Apollo lunar samples led the National Bureau of Standards to build several complete clean air laboratories dedicated to sample preparation wet chemistry. These laboratories were simple but effective in design and have been extensively copied by other laboratories. By the early 1980s, the issue of air quality (the Class of the clean air) was beginning to be recognized by many as less important than the other issue in clean laboratory design. That is, contamination reduction may depend as much or more on keeping gross quantities of analyte elements out of the laboratory and preventing the formation of undesirable corrosion products. This was not news for the geochemistry community, but by the 1980s it had become a mainstream problem for trace element analytical chemistry, primarily because of the new focus of analytical chemistry on environmental measurements. The question now is where does clean laboratory design go to exact further improvements in laboratory performance. Part of the answer may lie in examining other trends in analytical chemistry and projecting how a clean laboratory might accommodate them.

Introduction

Clean chemistry laboratories for the ultra-trace analysis of elements have become common, especially among those laboratories that work in the area of isotope geochemistry. However, back in the 1960s most analysts were still working in open laboratories. Most wet analysis was performed in glass apparatus using commercially available reagents equivalent to the American Chemical Society's (ACS) Reagent Grade. Elemental blanks from the reagents and apparatus alone amounted to more than a few micrograms. Some geologists were fortunate enough to be working with isotopes of elements of relatively low abundance. Few analytical chemists considered the environmental blank contribution to be a limiting factor in their analyses. Fortunately, isotope geologists were among the first to look for ways to lower the analytical blank since they were often limited in sample size or they were analyzing isotopic compositions at very low elemental concentrations. At the US National Bureau of Standards (NBS; now National Institute for Standards and Technology, NIST) in the late 1960s, scientists were measuring the elemental deposition from the air in the laboratories and they could easily find significant contaminations of 0.1-0.5 µg per day for elements like lead.

As the emphasis in inorganic analytical chemistry turned more toward trace analysis, analysts in many laboratories were discovering contamination problems in their measurements. The isotope geology laboratories and semiconductor electronics laboratories were the first to take positive steps to minimize contamination. Zief & Mitchell's (1976) book on contamination control was a real turning point in trace analysis for the general analytical community; it detailed procedures that had been in use at select laboratories for a number of years. A paper by Patterson & Settle (1976) represents another milestone in approaches to contamination control. Although both may be difficult to obtain now, they are superlative references since relatively little has changed in clean lab procedures from the principles presented by these authors. The NBS laboratories have published a guide to clean laboratory construction (Moody 1982) that has been widely used by many laboratories around the world. Although the basic design is still valid, we will try to project what the analytical clean laboratory might look like in ten years.

Historical Approaches to Contamination Control

The simplest approach to the control of contamination from laboratory air was to enclose the experiment inside a plastic box. Contamination was thus reduced to the amount of contamination contained within the box.

A more sophisticated approach was to use a filtered supply of nitrogen or another inert gas to flush the sample containment box and to keep it under a slight positive pressure. This prevented the influx of contaminants from outside of the box. Gloved ports were used for access to the sample. The major problem with this approach was the inconvenience involved. Dissolutions inside the box could be tricky and some sort of fume eradicator (a canopy to siphon off fumes) was necessary.

In the late 1960s and early 1970s, a few laboratories started to explore the use of clean air technology for application to the laboratory. The object was to overcome some of the difficulties of working in a closed system and still preserve the contamination control aspects in a new configuration. At this time, clean air was already extensively used in electronics manufacturing, medicine, and aerospace. The HEPA (High Efficiency Particulate) filters used were typically 99.97% efficient at 0.5 micrometer particle sizes. In an ordinary laboratory, a few filters could provide a huge improvement in the overall laboratory air quality and relatively high air quality in the designated clean bench area. Several of these designs were published (Patterson & Settle 1976; Zeif & Nesher 1974; Mitchell 1973). All required relatively stringent laboratory access procedures to keep the laboratory environment clean. None would meet strict air quality definitions but all were certainly useful.

An example of such a laboratory was the clean laboratory at the University of Ghent, Belgium. Designed by Versieck and Cornelis, the laboratory was used for their pioneering work on the analysis of trace elements in biological and clinical samples. Mitchell (1973) at the Bell Telephone Laboratories in the USA was another early pioneer in the development of a working clean laboratory for chemical operations. Typical clean air flow amounted to the equivalent of one room air change in a period of one to three minutes. NBS purchased a commercial clean room for chemical analysis in 1968 with much higher air flows, although nothing else in the laboratory was optimised for chemistry. This laboratory did not perform well for chemical applications. The greatest change in the approach to chemistry clean laboratory design probably occurred in 1971 at NBS when the inorganic mass spectrometry group built a new clean laboratory specifically for the analysis of the Apollo lunar rock samples. The adoption by NBS of a new approach to clean laboratory design would not have happened without the prior four years experience with a commercial clean room and the results observed in the efforts of other trace analysts.

The resulting NBS clean laboratory and its successor were described in detail by Moody (1982). These laboratories were simple but effective in design and have been extensively copied by other laboratories. By the early 1980s, the issue of air quality (the Class or cleanliness of the clean air) was beginning to be recognized by many as less important than other issues in clean laboratory design. That is, contamination reduction in a clean laboratory may depend as much or more on keeping gross quantities of analyte elements out of the laboratory and preventing the formation of undesirable corrosion products. This was not news for the geochemistry community, but, by the 1980s contamination and its prevention

had become a mainstream problem for trace element analytical chemistry, primarily because of the new focus of analytical chemistry on environmental measurements.

Present Day Clean Laboratory Design

At the present time, the International Standards Organisation (ISO) is preparing a new standard for the measurement and classification of clean air and other standards are also undergoing some revisions. At this time it is premature to quote new draft technical standards. These standards will harmonise nomenclature and clarify classifications of laboratories but the standards do not address real laboratory performance for chemistry applications. Technical standards aside, the actual quality of the HEPA filter has been improved greatly over the last twenty years allowing the air quality in the laboratory to be improved by a factor of one hundred or more over what was achievable in the early 1970s. The design of the filter has also improved, allowing the trace analyst to specify both a more efficient filter and metal-free filter body. It would be a mistake, however, to assume that improvements in the clean laboratory air quality have led to a corresponding improvement in the analytical blank.

Most of the earliest clean rooms for chemistry employed horizontal air flow. They also had a relatively small HEPA filter area relative to the volume or area of the laboratory. The NBS (NIST) design adopted a modified vertical flow industrial design. This approach required a total filter area, volume of air flow, and shortness of residence time for air in the clean laboratory that was significantly different compared to contemporary chemistry laboratories employing clean air. While the problems in chemistry applications are different from industry, the NBS (NIST) design shared more than a few common elements with industrial design. A deliberate attempt was made to keep the entire laboratory involved in the air circulation pattern to both reduce the residence time of the air in the laboratory and to effectively flush particles from the room that were produced by chemical processes.

Fume hoods were designed to handle perchloric acid in a laminar flow clean air environment. Whereas most industrial clean rooms operate at almost 100% recycling of the clean air, the NBS laboratory exhausted 35% or more of the total clean air through the fume hoods, thus reducing the recycled air to less than 65%. This meant that a high proportion of dirty make up air had to be introduced to the room to maintain the pressurisation of the laboratory. This created another break with traditional clean room design. With near 100% recycling, environmental controls (temperature and humidity) have to be built into the clean air handling system. It was not unusual to see facilities that devoted as much space to the installation of technical equipment as was devoted to the clean air space. This was expensive and wasted valuable laboratory space.

Because the NBS laboratories were retrofitted into existing spaces, all available space was at a premium. Consequently NBS turned to a system of modular clean air units that could be incorporated into the ceilings of existing laboratories. Since fume exhaust was to be about 35% of the total room air, the make up air normally provided

to the laboratory could handle all of the air conditioning and heating needed without having to modify any of the existing building air handling systems. The design was significantly cheaper than other approaches and over the years it has performed as well as or better than more conventional clean room designs. The entire sample handling areas have very high quality vertical laminar flow clean air which effectively isolates the samples from the analyst(s). All aspects of sample handling, dissolution, and separation were accommodated within the clean laboratory to eliminate the necessity of going in or out of the laboratory to perform another sample preparation step. The result of these and other factors such as ultra-purified reagents led to a substantial improvement (factor of 10 to 1000 or better) in the analytical blank in our laboratory and in others with similar operating conditions. Literally hundreds of copies of the laboratory have been constructed over the years with little change in the basic design.

The NBS (NIST) designers tried to provide the maximum performance for the least cost. However, despite the enormous improvements in measured air quality in the newest NIST clean laboratory, there has been little if any improvement in the analytical blanks attributable to the clean laboratory. Where blank reductions have been achieved, the results were through improvements in the analytical method, separations, or choice of reagents employed. The clean laboratory blanks seem to have been constant. One reason for this is that our laboratories are not totally metal free, leading to contamination by secondary causes such as touching or handling of artifacts in the laboratory that ultimately transfer to the samples when handled. Another reason is that to keep the laboratory as fully utilized as possible and to make its use attractive to staff, personnel hygiene restrictions have been relatively relaxed. Thus, improvements in procedures could be used to improve the laboratory performance even further. Nevertheless, the clean laboratory itself does not seem to be a major contributor to analytical blanks. Other factors such as ion exchange resins, reagents, and labware are larger contributors to the blank problem.

Recently, a few laboratories have attacked this one weakness of the NBS/NIST design clean laboratory. Two laboratories that have done an outstanding job of reducing secondary contamination sources (contamination not transmitted by the HEPA filter) are Boutron's laboratory in France (Boutron 1990) and De Bièvre's laboratory at the Institute for Reference Materials and Measurements (IRMM) in Belgium. Both laboratories have made extensive use of plastics to replace other materials of construction in the laboratory. The IRMM laboratory in Belgium is probably the ultimate achievement for the present clean air technology and laboratory design. Since the NBS or NIST designs are widely known and published, it may be more useful to examine how IRMM improved on the last NIST design. As with all discussions of clean laboratory design, the reader must judge the best design or feature for their application.

Planning for the IRMM facility began with NBS assistance in 1985 and continued for several years before a final design was accepted. All commercial clean rooms employ the principle of shelling or compartmentalizing clean operations inside of progressively cleaner environments. Patterson and Settle's (1976) chemical and sampling operations were based on the same principle, and these have been proven to be effective and necessary in instances of extremely low analyte concentration. Where the NBS laboratory employed zero or minimal progression into the cleanest environment, the IRMM facility has four distinct air quality zones starting with the complete isolation of the clean laboratory building from the adjacent mass spectrometry facilities. The laboratory facilities are classified as Class 1000, Class 100, and Class 10. Actual performance is better than specified.

The entire clean laboratory building at IRMM is physically isolated and supplied with HEPA filtered clean air. Although our experience at NIST has indicated that the HEPA filters may last for four to five years, there is little doubt that the relatively poorly filtered air supply to the NIST laboratories shortens the useful lifetime of the HEPA filters. The major justification for HEPA filtering for the entire building air supply at IRMM was that it would extend the clean laboratory HEPA filter life and also provide a high quality air supply for the building to further reduce the chance of contamination in the laboratories. Initially, this approach is expensive, but the redundant HEPA filter chambers used for the building air conditioning mean that the filters may be serviced or replaced with no interruption of service to the laboratories.

In addition to the highest level of air quality, all of the laboratory components are made of plastic or of materials that are fully protected from corrosion caused by wet chemical processes. The restrictions on use by laboratory personnel together with the modular design and metal free constructions go as far as seems possible towards reducing secondary contamination from the laboratory and from the chemists. The IRMM laboratory design probably represents the final stage of clean room evolution using conventional laboratory approaches. The question now is where does clean laboratory design go to extract further improvements in laboratory performance. Part of the answer may lie in examining other trends in analytical chemistry and projecting how a clean laboratory might accommodate them.

The Clean Laboratory of the Future

The largest consumer of clean room apparatus is the electronics industry. All of the clean laboratories in the world constitute an almost imperceptible fraction of the clean rooms constructed for the electronics industry each year. One may start with the premise that the only equipment that one can buy is the equipment that is manufactured for this industry. The medical industry is another large consumer of clean room equipment, but their equipment is still derived from the semiconductor market. One disturbing trend for analysts is a current trend in the semiconductor industry. With the ever decreasing size of microelectronic circuitry on chips, the demand for better air quality (ULPA filters, for instance) is leading to some manufacturing changes. In the 1970s we were careful to move from steel filter frames to aluminium frames and then to wood frames (metal-free) for the HEPA filters. With the demand for low particle counts, the wood frame is being phased out to accommodate the use of metal filter frames. Metals do not contract

or expand with temperature or humidity as much as wood. The reality is that we will have to adapt to the use of metal frames again over the next five years or so. This will create some problems in making these filters suitable for use in a trace metals laboratory. Particle counts will be lower, but much more care will be needed to protect the HEPA filter from corrosion.

The other trend that one may see in the electronics industry is a rapid adoption of automation to remove the human operator from the process. This in turn is leading to changes in equipment design and philosophy. In analytical chemistry, you may also see this trend with the rapid adoption of laboratory automation. The motivation for the laboratory manager may be to reduce laboratory costs more than to improve performance. Nevertheless, it is probably safe to assume that automation will become a majority factor in laboratories of the near future. Wet chemists with the knowledge to perform many laboratory operations are also disappearing.

Based upon these trends, this author speculates that the laboratory of the future will be built around automated apparatus. Further, it is likely that the most efficient way to do this is to adopt the semiconductor industry developed "mini-environment." The mini-environment is a fully self contained clean process with clean air, robotics, wet benches, *etc.* built into a closed chamber. These may be grouped and ganged together to perform sequential operations. They provide much better air quality with total isolation from the clean room in which the mini-environment is located. Ventilation and heating requirements may be greatly reduced since the environment provided is what the process needs, not what humans require. Chemists would have relatively little direct contact with a sample in this kind of clean room. Finally, there is one other advantage to the mini-environment approach. The cost is much less than would be needed to achieve similar process performance by conventional means.

If building a clean laboratory of about 100 m² today, one might spend well in excess of $(US)2,000,000. The cost for a clean room of similar performance utilizing mini-environments would be much less than half of that. Operating costs could be similarly cheaper for the minienvironment. Such a laboratory could not be built today since the automated laboratory equipment does not yet exist for many analytical operations. Finally, the analytical chemical process itself may be significantly improved with a more consistently clean operation without human intervention. No other large improvements in clean laboratory performance seem likely with the present design approaches.

References

Boutron, C F 1990 A Clean laboratory for ultralow concentration heavy metal analysis. Fresenius Zeitschrifter Analtische Chemfuerie 337:482-491.

Mitchell J W 1973 Ultra purity in trace analysis. Analytical Chemistry 45:492A-500A.

Moody J R 1982 NBS Clean laboratories for trace element analysis. Analytical Chemistry 54:1358A-1376A.

Patterson C C and Settle D M 1976 The reduction of orders of magnitude errors in lead analysis of biological materials and natural waters by controlling the extent and sources of industrial lead contamination introduced during sample collecting, handling and analysis. Proceedings of the Seventh Materials Research Symposium, US Government Printing Office, Washington DC.

Zief M & Mitchell J L 1976 Contamination Control in Analytical Chemistry. Wiley; New York.

Zief M & Nesher A G 1974 Clean environment for ultratrace analysis. Environmental Science & Technology 8:677-678