American Chemical Society
California Section

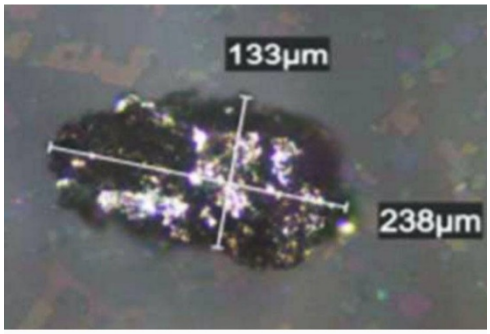
THE VORTEX

Volume LXXXIII
Number 9
November 2021
Newsletter

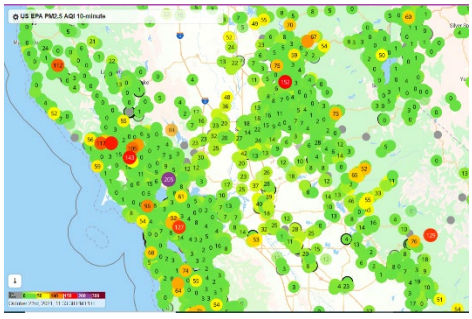
Twisted Oak Tree, taken at Taylor Mountain Regional Park, Santa Rosa

– Donald MacLean

CalSAFER
SAFER CONSUMER PRODUCTS INFORMATION MANAGEMENT SYSTEM



A particle of stainless steel found in Moderna Inc.'s COVID-19 vaccine | TAKEDA PHARMACEUTICAL CO. / VIA HEALTH MINISTRY / VIA KYODO



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Middle: Stainless Steel Particulate – The Japan Times, October 1, 2021;
Bottom. PurpleAir Map on October 23, 2021- https://map.purpleair.com

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MAGAZINE OF THE CALIFORNIA SECTION, AMERICAN CHEMICAL SOCIETY

Editor:
Donald MacLean
Donald.maclean.acs@gmail.com

Contributing Editors:
Nicki Davis
William Motzer

Office Administrator Manager:
Julie Mason
2950 Merced St. #225
San Leandro, CA 94577
510-351-9922
office@calacs.org

Editorial Staff:
Alicia Taylor
Alex Madonik
Jim Postma
Linda Wraxall
Al Verstuyft

web site: http://www.calacs.org

Chair's Message – Alicia Taylor

For our members living in the San Francisco Bay Area, many of us recently experienced a historic rain event in late October. In parts of Marin County, we received more than 12 inches of rain in approximately 24 hours! Hopefully our readers stayed safe and did not find any unexpected leaks in their residences. During storm events, I am reminded of the application of chemistry, even to rain, is very relevant. For example, the first big rain of winter removes all the gas, oil, and other accumulated chemicals (some from car exhaust) that have settled on the road over the past few months. Road runoff chemicals may alter water quality and may have physiological impacts to aquatic organisms once the road runoff enters streams. This is something I think about during every first rain event in the fall. For those of you who may be active in Citizen Science, I hope you were able to take some water quality measurements of local waterways before and after the rains. Over the past two years or so, Cal ACS has hosted more technical speakers on water quality issues. We hope to continue with this interesting topic – as always, you are welcome to suggest potential speakers for our events.

Some big news to share – Cal ACS won one ChemLuminary award! Our section won the Outstanding Women Chemists Local Section Event for our event featuring Professor Sherine Obare and her presentation on "Successful STEM Women of Color Must Network Differently". This was a joint event hosted by Cal ACS and East Bay AWIS. If you missed the event, a recording is available.

California Section
American Chemical Society

Women CHEMISTS Committee

All are welcome

Saturday, November 13, 2021

Title
A Career Journey in the field of Environmental Toxicology

Time
10:30 – 11:00 a.m.
Chatting

11:00 a.m.
Talk and Discussion

Reservation
Please visit the CalACS website www.calacs.org to register for this meeting or use Brown Papers Tickets. Link for registration:

https://www.brownpapertickets.com/event/5237987

Please register before Thursday, November 11, 2021, 12 PM. Your email address is needed to send the ZOOM link, which will be shared with attendees on or before the day of the event via Brown Paper Tickets.

Cost Free

About the Speaker

Alicia A. Taylor, PhD

Dr. Alicia Taylor is an environmental toxicologist and will share her career path (academia, consulting, government) with audience members. Dr. Taylor studied environmental toxicology, which included water chemistry, for her PhD at the University of California at Riverside.

She completed a postdoc at UC Berkeley, and then was an environmental science consultant for five years. During the pandemic, Dr. Taylor took a new job, and now holds a government scientist position at the California Department of Toxic Substances Control. Within the Safer Consumer Products Program, Dr. Taylor helps to reduce potentially toxic chemicals in consumer products.

Abstract

Dr. Taylor will cover her early education, what drew her to environmental chemistry, and in particular, environmental toxicology. She will share some tips for early career scientists on how to network, specifically on how to prepare for conference networking and the importance of volunteering in expanding one's network. She will give examples from her own participation in the CA section ACS. Dr. Taylor can be contacted via her LinkedIn profile.

Questions

Please contact Elaine Yamaguchi

eyamaguchi08@gmail.com

Bay Area Chemistry Symposium – 2021

By Patrick Lee

When: November 5, 2021 @ 8:30 am – 4:30 pm America/Los Angeles Time zone
Where: Virtual
Cost: Free
Email: bayareachemistrysymposium@gmail.com
Event website : https://www.bayareachemistrysymposium.com/

Please join us for the second Bay Area Chemistry Symposium. This event will be a virtual event over Zoom. Please register to receive a link.

The Bay Area Chemistry Symposium provides a unique opportunity to connect local students and academics with scientists from the pharmaceutical and biotechnology industries, covering themes of synthesis and design in medicinal, process, and computational chemistry. The one-day symposium will feature keynote addresses given by Gilead, Genentech, and Novartis as well as leading professors from the area and showcase research talks from graduate students, post-doctoral fellows, and industrial chemists. A poster session will also take place with presentations representing research conducted in both academic and industry laboratories. This symposium, co-chaired by Richmond Sarpong, Professor of Chemistry at UC Berkeley, and Kevin Allan, Director of Drug Substance Development & Manufacturing at Eidos Therapeutics, promises to be an exciting and influential community building event for synthetic, medicinal, and computational chemists across the Bay Area.

Register for this FREE event here: https://www.bayareachemistrysymposium.com/

Planned Section - Speaker: Prof. Daniel Snow - Nov 17

See Calacs.org website for information. No information provided as of press time.

Water Management in The Era of Climate Change: The California and Michigan Experience

When: Saturday – November 20, 2021 – 9:00 to 10:15 PM (PST)
Location: Online Zoom Event. See Calacs.org website for information.
Sponsor: Senior Chemist Committee

Attila Pavlath Legacy - 3

By Nicki Davis

This is the third installment of a series of articles about the life, career, and legacy of Attila Pavlath. Many of you know Attila through his service to the ACS, but know little of his life or his scientific career. The information in these articles will help fill that gap.

In this article, we learn how Attila took up his career after escaping to Canada and came to work at Stauffer Chemical in California.

Refuge in Canada — and a Miracle

Attila's research on fluorine chemistry was interrupted by the Hungarian Revolution of 1956, which was brutally suppressed by the Soviet Union. Attila and his family dodged machine guns and land mines to cross the border from Hungary into Austria, endured a 10-day ocean voyage to Canada on a converted freighter with several hundred other refugees suffering from seasickness, and, after a short stay in two Canadian refugee camps, moved in with his wife's relatives in Montreal, Quebec, Canada.

Attila tried to find work in Canada, but economic conditions in the country at that time made it difficult. Then came a stroke of luck that he calls a miracle: The vice president of research at a Canadian company wrote to him and told him that although the company wasn't hiring, they had a high regard and deep sympathy for Hungarian refugees. The company established a one-year postdoctoral fellowship for Attila at McGill University. The company said that if economic conditions in Canada improved in the intervening year they'd be happy to talk about a job, but on the other hand Attila would be under no obligation to work for the company if he found a position somewhere else. For someone who had left the refugee camp with only five dollars in his pocket, the position's $5,000 salary was a miracle indeed.

From Canada to America: Another Miracle

The postdoctoral fellowship at McGill University gave Attila a breathing space so he could look for a job in the USA. At this point his prospects for a job in the US didn't look good, because US immigration law at that time established quotas for different countries based on the percentage of the US population from that country in the census of 1910. Hungary had a quota of 900, which was already filled, and the waiting list was five to ten years. But then another miracle happened - an unintended gift from the Russians.

In October 1957, the Soviet Union launched Sputnik, the first artificial satellite. People in the US were shaken up by the realization that the US was lagging behind the Russians in science, so they were suddenly interested to get scientists from other countries to come to the US. It seems that youngsters in the US had been more interested in playing baseball and football than in studying science, but Sputnik changed all that. Moreover, Attila's research on fluorine chemistry was a hot topic at that time. There were two reasons for this.

One reason was the role of fluorine chemistry in the Manhattan Project, the work to create the first atomic bomb. Atomic bombs required the radioactive isotope uranium-235 (^{235}U), which had to be separated from the more common non-radioactive uranium-238. To separate the isotopes, uranium ore is converted to uranium hexafluoride, which is a gas. Gas diffusion can then be used to

separate molecules with different isotopes because $^{235}UF_6$ has a lower molecular weight than $^{238}UF_6$. The secrecy surrounding fluorine chemistry was one reason that Attila had found the literature on the subject so sparse when he was doing his PhD research in Hungary.

Another reason for the interest in fluorine chemistry was its use in solid fuel for rockets. Elemental fluorine is a good oxidizer, but requires low temperatures to put it in liquid form, so the idea was to try to convert the oxidizing power of the fluorine by combining it with various complexes to make solid oxidizers. Attila's doctoral dissertation in Hungary described how to use fluorine in organic reactions without the risk of explosions.

As a result, companies that were doing fluorine chemistry were very interested in Attila. He applied to several companies in the United States doing research in fluorine chemistry and received several interview invitations in New York, Cleveland and St. Paul which were quickly followed by job offers.

While he was pondering which one to select, he was unexpectedly approached by Stauffer Chemical, a manufacturer of organofluorine agrochemicals in Richmond, California, to fly out for an interview. Attila was intrigued: This company had actually reached out to him, instead of the reverse! At that time California was not known to be involved in large scale chemical research. Anxious to resume his pioneering scientific career, Attila accepted their offer to fly across the country for an interview.

So, on a February day in 1958, Attila landed at Oakland Airport in California. He was coming from an environment of three-foot-high snow drifts, wind, and -20 degree temperatures in Montreal to a location where the sun was shining and temperatures were 75-80 degrees. "I was dressed like an Eskimo, and people there were dressed in short-sleeved shirts," he recalled.

Attila didn't want to show too much enthusiasm, but company representatives were trying hard to persuade him to take the job. One of their concerns was that scientists might be reluctant to work on the West Coast because of lack of opportunities for professional development; there wasn't much science on the West Coast at that time, and a flight to the East Coast was ten hours by propeller plane. A company employee from Ohio told Attila that Ohio did have more science, but assured him that Stauffer treated its scientists well and sent them to a meeting on the East Coast at least once per year.

Attila didn't want to tell them that he'd already decided when he landed. He recalls, "I actually phoned my wife when I checked into the hotel saying, 'I don't know what they are going to do, but if they offer anything, you can start packing because we're moving.'"

After completing his interview, the company offered Attila a job, and he said he would consider it. As soon as he returned home he phoned the company and said "Yes." Then he brought up the issue of his immigration status and the long waiting list for immigrants from Hungary. The company asked their representative in Washington for help, and within a week, Attila got a call from the American Embassy in Montreal asking him to please come in to process his visa. He was given first preference in the quota because Sputnik had created such a demand for scientists that the American authorities side-stepped the quota. Attila received his Green Card a week after his visit to the embassy in Montreal, and was riding on a plane to California.

So, thanks to the Russians and the Sputnik miracle, Attila began his career in the USA.

Fanny Frausto - ACS Industry Matters Newsletter

Fanny Frausto was showcased in Industry Matters Newsletter, September 30, 2021, titled "**Meet a designer of cleaning product formulations with high ambitions"**. The issue she reveals the indispensable roles a teacher, her dad, and scholarships have played in her career. She is the current Cal ACS section Chair-Elect, and works at The Clorox Company.

Shout Out – Awards and Announcements

2021 Cal ACS Section Election Slate

Compiled By Jim Postma

The following are the Cal ACS local section Election Slate as of October 25, 2021. Election notice will go out in October.

Position	Positions Open	Nominee(s)
Councilor	2	Eileen Nottoli and Jim Postma
Chair-Elect	1	Atefeh Taheri
Treasurer	1	Paul Vartanian
Member-at-Large	4	Charles Gluchowski
Director-at-Large	1	Attila Pavlath, and Lee Latimer

Cal ACS WCC Wins ChemLuminary Award – Outstanding Local Section Event

By Alex Madonik

Cal ACS and East Bay AWIS co-hosted Dr. Sherine Obare on 04 August 2020 for this award-winning event. Her theme was "**Successful STEM Women of Color Must Network Differently**." **Here is the recording of the event.**

We were also finalists for the Outstanding Local Section Industry **Event** for another virtual event co-organized with AWIS East Bay, featuring Dr. Kirk Nass of Chevron. **Here is the recording of that event.**

Additionally, we were finalists for **"Outstanding Performance Awards – Large Size Category"** and **"Best New Senior Chemists Activity within a Local Section."** Other sections won these awards, but we were honored as finalists.

Congratulations to the Women Chemists Committee and to Outreach Volunteer of the Year Atefeh Taheri!

Lee Latimer Re-elected to Another Term on ACS Board

Lee Latimer has been re-elected to another 3 year term to the ACS Board. He serves with another section member, Bryan Balazs.

History

All That Glitters…?

Part 7

By Bill Motzer

By 1852, most artisanal placer gold mining in the Mother Lode's (ML) streams and rivers was over, so in 1853 gold miners developed more efficient industrial hydraulic mining methods capable of recovering gold from "dry" alluvium also known as paleo-placers (Figure 1). One of the most famous of these sites is at Malakoff Diggins, mined by the North Broomfield Gravel Mining Company (Figure 2) for 44 years. However, this hydraulic mining method was curtailed by the now famous January 1884 Judge Sawyer injunction prohibiting hydraulic mining. It's now a California State park and may be visited by driving 42 km (26 miles) northeast from Nevada City (Figure 3). To obtain the necessary hydraulic pressures, miners dammed Sierra Nevada streams, rivers, and alpine lakes, constructed elaborate long pipelines, and dug trenches to bring water to the appropriate paleo-placers. At Malakoff Diggins, pressures were intensified by seven large metal monitors (Figure 4) that directed flows. However, this type of mining resulted in considerable environmental impacts with subsequent detrimental consequences.

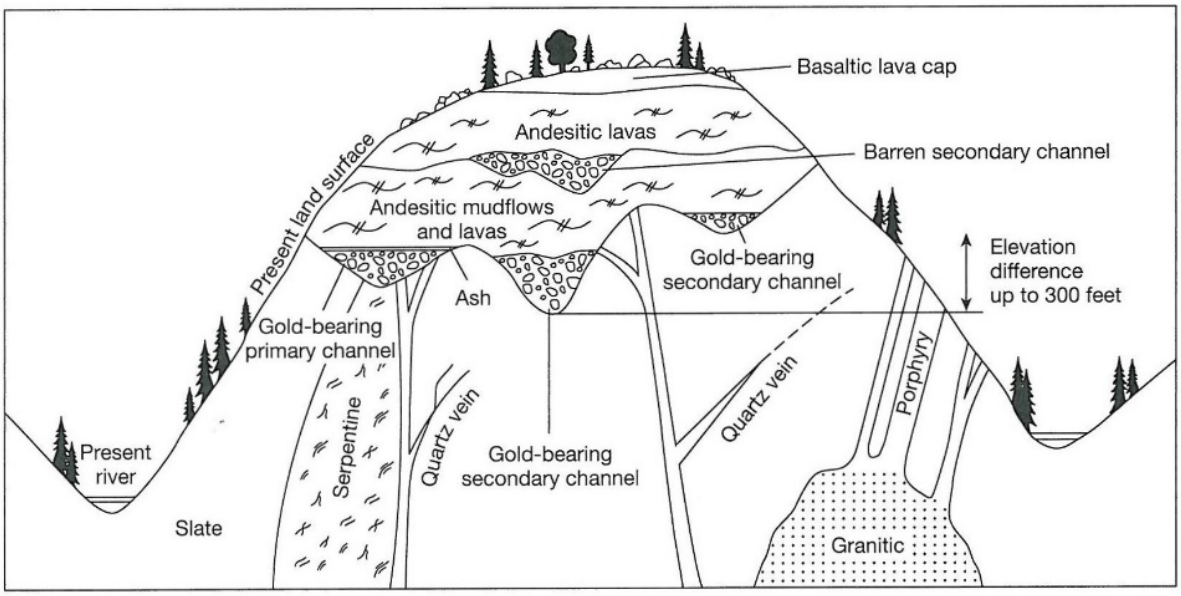

Figure 1: Cross section model showing different gold deposit types. Paleo-placers occur in gold-bearing primary and secondary channels that were hydraulically mined. Source: J. Chakarun, 1988, *California Geology* magazine.

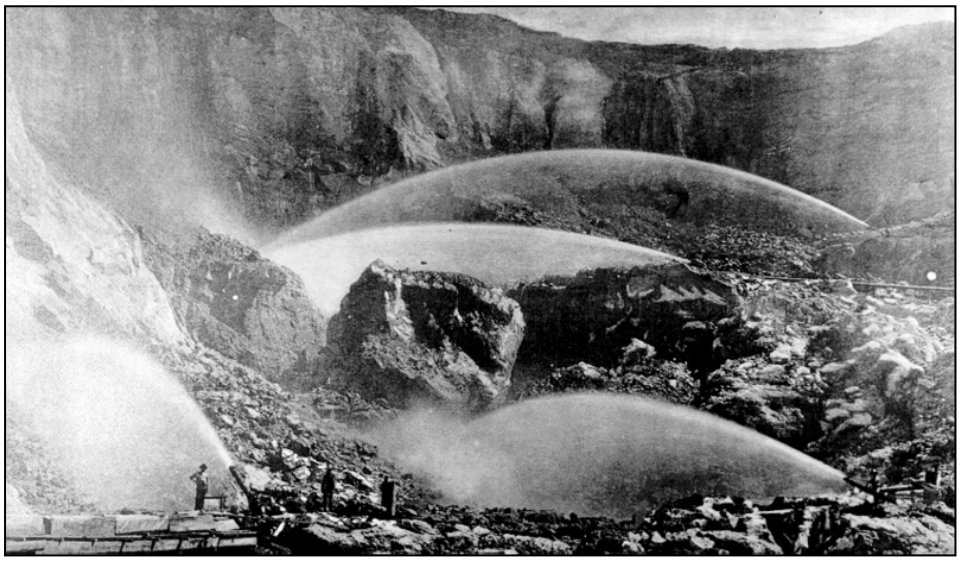

Figure 2: Malakoff Diggins: circa 1860, showing active hydraulic mining. Source: Watkins Photo Bancroft Library Neg.#8111. Unknown Author.

Figure 3: Malakoff Diggins State Historical Park. View of “pit” and remaining paleo-placer deposits in “cliff”. Photo by W.E. Motzer, August 2011.

Figure 4: Large monitor on display at Waukeshaw Drift Mine, Relief Hill, CA. Photo by W.E. Motzer, October 2009.

The "Physical" Consequences

Prior to the Gold Rush, San Francisco's (SF) bays (from NE to SW-S, respectively: Honker, Grizzly, Suisan, San Pablo, Richardson, Central, and South Bay) average depths are estimated to have ranged from 30 to 40 ft (10-15 m) (Figure 5) and most SF Bay sediments were composed of sand. However, hydraulic mining produced massive quantities of washed gravel, sand, silt, and clay, estimated at 191.14 million cubic meters (see Part 5 in the September 2021 Vortex for more details) that flowed into rivers eventually reaching SF Bay. These "slickens" (largely silt and clay) filled much of the shallow shoreline flats, raising the entire SF Bay profile, creating new marshes. By 1883, SF Bay was filling at the rate of 1.0 ft/yr (0.3 m/yr), The current average depth is ~12 to 15 ft (4 to 5 m). In the Hayward – San Mateo to San Jose area of South Bay, depth ranges from 12 to 36 in (30 to 90 cm). Because of tidal flow/surges, the deepest part is just outside of the Golden Gate at ~372 ft (31 m) (Figure 6).

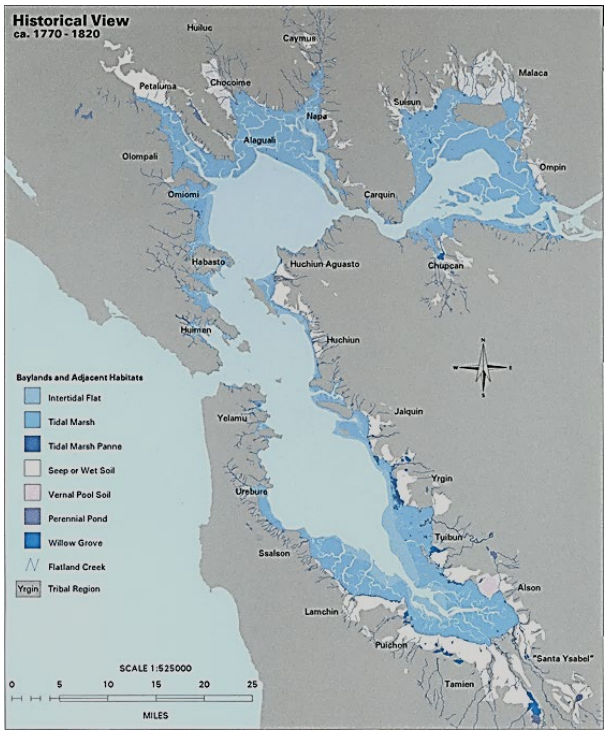

Figure 5: SF Bay postulated configuration prior to the Gold Rush: circa 1770-1820, also showing Indigenous Peoples sites. Source: U.S. Geological Survey.

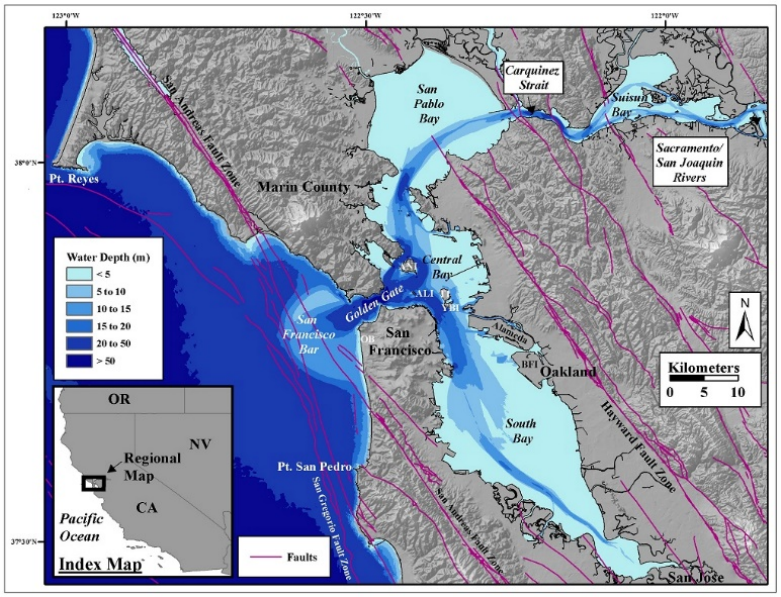

Figure 6: Modern (current) SF Bay depths in meters. Source: P.L. Barnard, 2013, *Marine Geology* special issue, v. 345.

The "Chemical" Consequences

Based on investigations, studies, and research, that I was involved with or aware of, the fine silts and clays in SF Bay sediments sorb and retain contaminants, including:

- Polycyclic biphenyl compounds (PCBs) from industrial sources and possible surface releases, including transformer fluid releases and disposals.
- Lead from pealing white and red lead-based paint used on sailing ships and other boats.
- Tributyl tin oxide, an organotin compound in the $(C_4H_9)_3$ Sn group painted on boat bottoms as an antifouling agent.
- Oil and grease from boats, ships such as oil tankers, and refinery spills from SF Bay area refineries.
- Native mercury and gold – mercury amalgam washed in from the hydraulic mining and from adjacent mercury mines in the Coast Ranges. And I'll discuss the mercury mines, their geochemistry, and environmental impacts in my next article.

Employment Opportunity at the California Department of Health

The California Department of Public Health is hiring! Positions focused on chemical sciences and public health laboratories include Examiner I, II, III, Research Scientists I-IV, Research Scientist Supervisors & Managers and are located throughout California.
The state has a three-step application process:
1) Create a CalCareer account;
2) Take the appropriate examination(s)/assessment(s) and;
3) Apply for jobs.

The above positions hyperlink to the exam bulletins which will outline the minimum requirements. Current vacancies are listed on the CDPH Career Opportunities pages. For assistance with the application process, please contact our recruitment team via email at apply@cdph.ca.gov.

Editor's note: this was provided with links. Web address was added in case the links did not work or if this was printed.

https://www.calcareers.ca.gov/CalHrPublic/Exams/Bulletin.aspx?examCD=8H1AU01
The link to examiner II was the same as examiner II.
https://www.calcareers.ca.gov/CalHrPublic/Exams/Bulletin.aspx?examCD=6H1CH
https://www.calcareers.ca.gov/CalHRPublic/Search/ExamSearchResults.aspx#kw=research%20scientist
https://www.calcareers.ca.gov/CalHRPublic/Login.aspx
https://www.cdph.ca.gov/Programs/HRB/Pages/HumanResourcesBranch.aspx

Teaching Moment

Nomenclature is the Number One Safety Quality Aspect – Part 2

By Donald MacLean

Part 1 introduced the reasoning behind pharmaceutical nomenclature and the organizations responsible for creating and assigning names. In installment 2 monoclonal antibody, cell and gene therapy, and vaccine nomenclature will be discussed and how the nonproprietary name is based on its initial function / mechanism.

Antibodies Have Nonproprietary Nomenclature Complexities

Monoclonal antibodies have a terminal -mab stem. Polyclonal antibodies mixtures from mab pooling have a terminal -pab stem. In combination products where 2 or more antibodies are manufactured separately and then mixed, each component receives a separate USAN ending in –mab. Unlike their small molecule counterparts, antibodies have infixes (substems) that refer to their target and source.

Example:

1. Hemlibra ® (by Genentech, approved 2017) nonproprietary name is emicizumab-kxwh used for Hemophilia A.
2. Ebanga ™ (by Ridgeback Biotherapeutics, approved 2020) is ansuvimab-zkyl to treat Ebola.

Prefix: emi- and ans-
Infixes: -ci- = cardiovascular, -zu- = humanized, -vi- viral
Terminal Stem: -mab = monoclonal antibody
Biological Qualifier (BQ): kxwh and zkyl

If the product is radio-labelled or conjugated to another chemical, such as toxin, conjugate identification is accomplished by a separate second word or acceptable chemical designation. If the monoclonal antibody is used as a carrier for a radioisotope, the latter will be listed first in the INN, e.g. technetium (99mTc) pintumomab.

Antibodies collected from blood are polyclonal. However, the polyclonal terminal stem (-pab) usage is reserved for monoclonal mixtures. Polyclonal antibodies have polyvalent (or polivalent) second word. A special type of antibody product is the hyperimmune (also known as convalescent plasma) globulin is a licensed product that is manufactured from convalescent plasma from a large number of donors.

Example: antivenin crotalidae polyvalent is a treatment for snake bites made from preparation of polyvalent equine immunoglobulin.

Table 4 lists infixes for monoclonal antibodies. There is pre 2017 and post 2017 stems.

Table 4. Nonproprietary Stem for Monoclonal Antibodiies - source Biologicals 2019

Source Substem			Target Substem		
Until 2017 Substem (Infix)	Post 2017 Substem	Source	Until 2017 Selected Target Substem	Since 2017 Target Substem	Directed toward
			-am(i)-	-ami-	Serum amyloid
-a-	-a-	rat	-ba(c)- -b(a)-	-ba-	bacterial
-axo-	-axo-	Rat-mouse	-ci(r)- -c(i)-	-ci-	cardiovascular
-e-	-e-	hamster		-de-	Metabolic or endocrine pathways
-i-	-i-	primate	-fung- -f(u)-	-fung-	fungal
-o-	-o-	mouse			endocrine
-u-	-u-	human	-gr(o)-	-gros-	Skeletal muscle mass related growth factors
-xi-	-xi-	chimeric	-ki(n)- -k(i)-	-ki-	interleukin
-zu-	-zu-	humanized	-l(i)-	-li-	immunomodulating
	-xizu-	Chimeric / hmanized hybrid	-n(e)-	-ne-	neural
			-os- -s(o)-	-os-	bone
			Many -t(u)-	-ta-	tumor
			-tox(a)-	-toxa- -vet-	toxin (conjugated to a toxin) veterinary
			-vi(r)- -v(i)-	-vi-	viral

Gene Drugs Have Even More Complexities

Gene therapies have a 2-component nomenclature with prefix + infix + suffix structure. Word 1 is the gene component, and word 2 is the vector component.
Word 1: (random) + (gene) + ("[a vowel]gene")
Word 2: (random) + (viral vector) + (suffix)

Table 5 shows the gene therapy stems.

Table 5. Gene Therapy Stems			
Word 1 gene infix	Word 2 Infix 1	Word 2 Infix 2	Word 2 suffixes
-cima- : cytosine deaminase	-adeno- : adenovirus	-tu- tumoricidal	-vec : non replicating viral vector
-naco- : coagulation factor IX	-cana- : canarypox		-repvec : replicating viral vector
-far- : interferon	-foli- : fowlpox		-bac : bacteria vector
-ermin– : growth factor	-erpa- : herpes virus		-plasmid : plasmid vector
-kin- : interleukin	-lenti- : lentivirus		-rev : therapeutic virus
-lim- : immunomodulator	-morbilli- : paramyxoviridae		
-lip- : human lipoprotein lipase	-parvo- : adeno-associated virus		
-mul- : multiple gene	-retro- : other retrovirus		
-stim- : colony stimulating factor	-vaci- : vaccinia virus		
-tima- : thymidine kinase	-lis- : listeria monocytogenes		
-tusu- : tumor suppression			

Example:

1. talimogene laherparepvec (Imlygic by Amgen) a modified oncolytic viral therapy for melanoma (-lim- imunomodulator; -erpa- herpes virus, -repvep replicating viral vector)
2. voretigene neparvovec-rzyl (Luxturna by Sparks Therapeutics) an adeno-associated virus 2 for Leber congenital amaurosis (inherited retinal disease)(-parvo- aav, -vec non replicating viral vector, rzyl is the biological qualifier)

Cell Drugs are Also Complex

Cell therapies have the “-cel” terminal stem. Prefix + infix 1 + infix 2 + suffix or (random) + (manipulation) + (cell type) + (“-cel”).

Prefix: Cell type: Auto- autologous; allogenic – taken from different individual from the same species; xenogenic – taken from different species

Infix 1 manipulation: -fus- fusion to a cell

Infix 2 cell type: -co(n)- chondrocytes; -cor- umbilical cord cells; -defitem- differentiated stem cells; -den- dendritic cells; -end(o)- endothelial cells; -ep(a)- hepatocytes; -fi(b)- fibroblasts; -isle- islet cells; -ker(a)- keratinocytes; -leu- lymphocytes/monocytes/APC(white cells); -mestro- mesenchymal stromal cells (msc); -mio(b)- myoblasts; -ova- ovary cells; -pla(c) placenta cells; -ren- renal tubular cells; -ret- retinal epithelial cells; -tem- for stem cells; -tesi- testis cells; -tu- or -tucel- tumor cells, -ur- urothelial cells.

Example cell therapy:

1. axicabtagene ciloleucel (by Yescarta by Kite Pharma, Inc.) an autologous T-cell : -cabta- cell expressed antibody and T cell activation, -gen gene, -leu- white cell, -cel cell based

2. tisagenlecleucel (Kymriah by Novartis) autologous Car T Cell for leukemia (lentiviral).

3. spanlecortemlocel (by Magenta Therapeutics) an allogeneic umbilical cord blood haematopoietic stem cell for bone marrow transplant.

RNA

A new class of drugs involve nucleic acids. One such is antisense which has -rsen terminal ending. mRNA Covid 19 vaccines have -meran terminal stem. Table 6 shows the suffixes for RNA drugs.

Table 6. RNA Nonproprietary Stems	
suffix	Designate
-rsen	antisense oglionucleotide
–nersen	neurological disorders antisense oglionucleotide
–dirsen	muscular dystrophies antisense oglionucleotide
–virsen	antiviral antisense oglionucleotide
-meran	Messenger RNA
-siran	Small interfering RNA's (siRNA)

nusinersen (Spinaza® bylonis Pharmaceuticals) for spinal muscular atrophy; -nersen neurological disorder
patisiran (Onpattro™ by Alnylam) for polyneuropathy. -siran indicates that this is small interfering RNA mechanism.

Vaccines:

Vaccines have received a lot of attention due to the Covid 19 pandemic. Vaccines can be made from a number of sources and may combine all of the aforementioned nomenclature schemes and a number of others depending upon their source and action. Because Covid 19 vaccine development is recent some of the vaccines have not been assigned a USAN / INN / JAN name. For the Prizer and Moderna RNA vaccines, the terminal stem is -meran.

Table 7. Covid 19 Vaccines Example		
Brand Name and Manufacturer	USAN / INN or other name	Stems / comment
Comirnaty By Pfizer-BioNTech	Tozinameran (viral)	Tozina- prefix -meran mRNA immunization
Spikevax By Moderna	Elasomeran (mRNA encapsulated in lipid nanoparticles	-meran mRNA immunization
J&J *COVID*-19 vaccine By Johnson and Johnson (Janssen)	(Ad26.COV2-S [recombinant]) (Adenovirus (Viral vector), inactivated)	Recombinant, replication incompetent adenovirus type 26 (AD26) vectored vaccine encoding the (SARs-CoV-2) Spike (S) protein
Covishshield and Vaxzevria By Astra Zeneca	*(ChAdOx1-S [recombinant])* (viral vector)	Unknown by author
Covovax By Novavax	Recombinant nanoparticle protein based (protein subunit and virus-like particle)	Unknown by author
CVnCoV By CureVac (withdrawn application)	Zorecimeran mRNA based vaccine encapsulated in lipid nanoparticle (LNP) [provisional]	-meran mRNA immunization

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Selected Industry News

Japan's Moderna Covid Vaccine Had Black Stainless Steel Particles – Recall Product

Initial 100% Visible Particulate Inspection a Requirement

By Donald MacLean

The news from Japan in August for Moderna's Covid 19 vaccine was shocking (Sold by Takeda Pharmaceutical Company Ltd.). At first there was just the story line. The initial suspect was piece of the stopper. But as time passed the black particulate was identified as metallic stainless steel (Grade 316). In the food production sector X-rays are used to detect metals in packaged goods, but with pharmaceuticals this may be impractical. Unlike sterility, aggregation and glass delamination that can develop with storage, metal particulates come from the manufacturing process or at the time of use. Pharmaceutics use initial 100% visual inspection, if practical, either manually or by machine

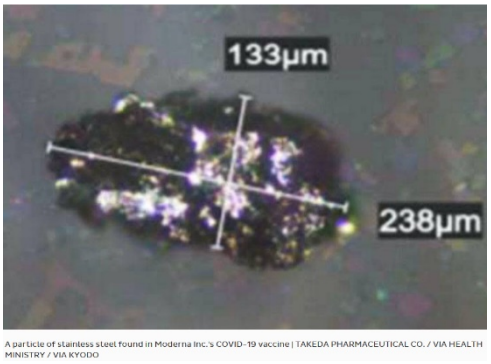

Figure 1. Image snipped from The Japan Times, October 1, 2021 showing black particulate. Note the size.

Figure 2. Image snipped from Satish K Singh presentation at USP Workshop on Particulates,
Control and Determination of Visible and Sub-visible Particulate Matter in Biologics, June 26-27 2017.
Mathonet et al., PDA JPST, 70, 392, 20

inspection. Any findings are classified as critical, major, and minor. Visible particles fall into the major category. Pharmacopeia have limits on subvisible, and visible particulates, and to some extent submicron particles.

Spotting visual particulates is not easy and requires Operator eye testing qualification using single particulate testing standards in the same inspected container type and Operators' eye examination. Qualification and validation of inspection process descriptions can be found in USP <1790> "Visual Inspection of Injections". Manual inspection procedures (light intensity and background) are described in various compendia, including USP <790> "Visible Particulates in Injections".

USP, EP, and JP (United States Pharmacopeia, European Pharmacopeia, Japanese Pharmacopeia) have visual inspection procedure requirements that are similar, but differ in their definition of allowable visible particles and their inspection approach. I will use USP as an example of visible particulate inspection and reference JP as needed since this observation happened in Japan, but the product made by a US company. USP has taken the approach of practically particulate free using a statistical approach upon a second visual inspection since USP 39-NF 34 (<790> on May 1, 2016) then added an informational chapter in USP 40 – NF-35 (<1790> on May 1, 2017). This statistical approach is being applied with EP but not JP (as of JP 17 as JP 18 is not available in English translation).

In the *United States Pharmacopeia* (USP) the overarching general chapter based on dosage form is general chapter <1> Injections and Implanted Drug Products (Parenterals)—Product Quality Tests directs what tests apply. It has three basic sections, universal tests, specific tests, and dosage form based tests. It lists <790> "Visible Particulates in Injections", and <1790> "Visual Inspection of Injections" which contains a reference to an external organization for criteria based on lot / batch size and acceptance quality level. USP requires "Essentially free" of visible particles based upon post 100% manufacturing inspection statistical reinspection. What this means is that low quantities of visible particles are allowed under a set of circumstances.

In the European Pharmacopeia general chapter (EP) 2.9.20. "Particulate contamination: Visible particles" and EP 5.17.2. "Recommendations on testing of particulate contamination: visible particles" (effective date 2021-01-01, new chapter), used the term "Practically free from visible particles". EP uses a statistical reinspection approach like USP, meaning low amounts of visible particles are allowed under a set of inspection criteria. However, EP also has a monograph 2031 on Monoclonal antibodies for human use (effective date January 2012), where monoclonal antibody preparations are "without visible particles, unless otherwise justified and authorized." under the appearance test section. This conflict has not been resolved and has caused consternation when dealing with EP.

In the *Japanese Pharmacopoeia* (JP 17th edition) the general chapter is <6.06> "Foreign Insoluble Matter Test for Injections" (effective date 2016-04-01) has "Injections or vehicles must be free from readily detectable foreign insoluble matters.".

The following are the steps needed to be done for visual inspection.

Initial 100 % Visual Inspection and Partial Re-inspection

Start with 100% initial visual inspection for all manufactured samples if possible. This is the culling step for those drug product containers that do not meet esthetics, particles, color, etc. If the nature of the sample or container closure system does not allow for 100% inspection, then a portion of the samples in the batch are subject to destructive testing. This could mean reconstituting freeze-dried product or transfer material from a colored container to a transparent container for visual inspection.

After the culling step for those that can be directly analyzed, perform visual inspection for those samples that passed the initial 100% inspection this time with defect classification scoring. The compendia state how this is to be performed. Refer to ANSI/ASQ Z1.4 (or ISO 2859-1) for Sample Size Letter Codes. There are 3 general inspection levels (1 most stringent, 2, and 3 least stringent) and 4 special inspection levels (S-1, S-2, S-3, and S-4). The number of manufactured samples will yield a letter code for each general inspection level. That letter code is then used in another reference table and read to the right until getting to the AQL (acceptable Quality Limit) column desired. In Table 1, the number of samples to be reinspected is stated based on initial batch size with a 0.65% AQL. Here General Inspection level 2 is used with a AQL of 0.65% (can use a smaller AQL value, meaning even more rigid passing criterion). As an example, if AQL is 0.65% and a 10000 vial lot was manufactured, 200 vials are reinspected. Up to 3 vials with major defect can be allowed. Critical defects are not allowed.

AQL means the poorest level of quality that is considered acceptable in a particular population or in a pre-defined sample size. For example: “AQL is 0.65%” means “I want no more than 0.65% defective items in the whole order quantity, on average over several production runs with that supplier”.

Sampling at Batch Release (After 100% Manufacturing Inspection)

Sample and inspect the batch using ANSI/ASQ Z1.4 (or ISO 2859-1). General Inspection Level II, single sampling plans for normal inspection with an AQL of 0.65%. Alternative sampling plans with equivalent or better protection are acceptable. NMT the specified number of units contains visible particulates.

Table 1. Sampling at Batch Release (after 100% Manufacturing Inspection)

Follow General Inspection Level II. The sample letter code comes from Lot or Batch size and the Special or General Inspection Level. The Sampling letter Code is then used in another table to determine sample size and the acceptance and rejection number for selected AQL.

Table 1. Inspection Level II Single Sampling Plan

	(Sampling Letter Code) Accept Number, Reject Number/Sample Size		
Lot Size	AQL 0.10%	AQL 0.25%	AQL 0.65%
151 to 280	(G) 0,1/32	(G) 0,1/32	(G) 0,1/32
281 to 500	(H) 0,1/50	(H) 0,1/50	(H) 0,1/50
501 to 1200	(J) 0,1/80	(J) 0,1/80	(J) 1,2/80
1201 to 3200	(K) 0,1/125	(K) 0,1/125	(K) 2,3/125
3201 to 10000	(L) 0,1/200	(L) 1,2/200	(L) 3,4/200
10001 to 35000	(M) 0,1/315	(M) 2,3/315	(M) 5,6/315
35001 to 150000	(N) 1,2/500	(N) 3,4/500	(N) 7,8/500
150001 to 500000	(P) 2,3/800	(P) 5,6/800	(P) 10,11/800
>500,000	(Q) 3,4/1250	(Q) 7,8/1250	(Q) 14,15/1250

Table 2. Typical 0.65% AQL (Acceptance Quality Limits) sampling schemes for normal, single-pass inspection using S-3 and S-4 levels, dependent upon lot size. (PF 46 (6) Nov-Dec 2020 proposal to USP 1790 table 2, not incorporated May 1, 2021 effective date version).

Table 2. AQL Values for Visual Inspection – source USP <1790>		
Defect Category	AQL Range	Defect Example
Critical	0.010 to 0.10%	may cause serious adverse reaction or death - Container integrity
Major	0.10 to 0.65%	risk of a temporary impairment or medically reversible reaction - Impairment to product use
Minor	1.0 to 4.0%	do not impact product performance or compliance - Cosmetic appearance or pharmaceutical elegance.

There are times when 100% inspection is not practical such as opaque containers. In this case a small set of samples are sacrificed. Another case might be when sample are on stability.

Table 3. Second Inspection Criteria

	(Sampling Letter Code) Accept Number, Reject Number/Sample Size					
	0.10% AQL for Critical Defects		0.65% AQL for Major Defects		4.0% AQL for Minor Defects	
Lot Size	Inspection Level S-3	Inspection Level S-4	Inspection Level S-3	Inspection Level S-4	Inspection Level S-3	Inspection Level S-4
200–10,000	(F) 0,1/20	(G) 0,1/32	(F) 0,1/20	(G) 0,1/32	(F) 2,3/20	(G) 3,4/32
10,001–500,000	(G) 0,1/32	(J) 0,1/80	(G) 0,1/32	(J) 1,2/80	(G) 3,4/32	(J) 7,8/80
>500,000	(H) 0,1/50	(K) 0,1/125	(H) 1,2/50	(K) 2,3/125	(H) 5,6/50	(K) 10,11/125

The following is an example of a two-stage test plan as described above: Using an S-3 plan for a batch size of 100,000 units, the initial sample size is 32, with accept on 0 and reject on 1. If 1 unit is found with a visible particle, the S-4 (stricter) plan may be selected, and the new sample size of 80 (initial plus additional sample) may be used. An additional 48 samples are then tested and, if no further evidence of visible particles is detected, the batch meets the acceptance criterion (from PF 46 (6) with corrections on sample size values as the print had errors). The results from the samples must be combined, rather than resampling and basing the accept decision on the results of the second sample only.

Products in distribution

Chapter <790> provides that zero particles found in the sampling and inspection of 20 units signifies that the batch is “essentially free of visible particulates.”

Typical sampling plans for this type of test can be found in the special sampling plans S-3 and S-4 in ANSI/ASQ Z1.4 which can be purchased.

Commentary

So how did the black particles slip by visual inspection? If visual inspection was done manually, the answer is easy as Operators get tired, and the particulate size is at the lower edge of the visible particle size detectability. In this case the inspection was performed by automated machine by the Spanish manufacturer, so those issues do not exist. However, machines need proper programing, resolution, and acceptance limits, which may have been a problem here. The inspection scheme followed uses the requirement meant for the country / region where the product is meant for.

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REVIEW

Travel Photos

Its Salt, Its Sand, Its Snow, no its Detergent?

Chemistry in Action: It started to rain. White stuff collected on the street gutters. My first thought was salt. Then the roadway turned white, that is when I thought sand was dumped on the road because first rains make the road slippery and sand is a good fix for slipperiness. I turned left and the road was really white. At the stop light the road looked like snow, but there was no snow on the windscreen or anywhere else. It was 50 F. At the next light I really took a look, realizing it was foam. The city had put detergent on the both sides of the main roads for the first rains (McDowell Blvd, Petaluma. October 17, 2021). – By Donald Maclean

Meeting Review

Fall WCC Seminar: "Air Pollution in High Definition: Building Low-Cost Sensor Networks & Community Partnerships"

By M.T. Cheng

On September 18, 2021, Dr. Alexis Shusterman and Dr. Chelsea Preble executed a tag-team presentation for the Women Chemists Committee quarterly seminar. They presented the need for higher spatial resolution in the understanding of air pollution, through the installation of many low-cost monitoring devices, and in particular, the need to involve the community where the measurements are taken. The focus is at the areas where there are large proportions of socioeconomically disadvantaged residents.

Alexis began with some background on air pollution; the pollutants are gaseous species such as ozone, carbon monoxide, and oxides of nitrogen; and more importantly, particulate matters in the SF Bay Area. Areas near a roadway are typically laden with high concentrations of pollutants, and there are large proportions of disadvantaged residents near roadways. In addition to the social and political injustices burdening this group, reducing environmental injustice presents unique challenges and requires specially tailored efforts. To implement mitigating measures, it is necessary to know to a much higher resolution where the pollution is most severe, as well as, the source of the pollutants.

Alexis followed with discussions on strategies and mechanisms in the measurements of these pollutants; highly accurate speciated measurements versus the affordable high-density measurements. Examples are the BAAQMD measurement sites, and the very prevalent PurpleAir monitors (editor's note this is a brand that measures particulates numbers using a laser, converting the size to mass, then size binning. This is different collecting particulates on filters for a set period then weighing the filters. Both methods suffer from particulate density affecting results.). The choice is dictated by the local "ecology" and the questions needing an answer.

Chelsea was then tagged to describe the creation of the black carbon, or soot measurement device, known as Aerosol Black Carbon Detector (ABCD), which is a collaboration of UCB/LBNL, regulatory agencies, and community organizations. One hundred of these devices were installed in the area encircled by Interstate 880 to the west and south, Interstate 980 to the east, and Interstate 580 to the north. This area is the home of many Black and Brown people, while simultaneously used by the Port of Oakland, train depot, and trucking companies. The data of the one hundred devices were gathered for one hundred days in the summer of 2017.

In the summer of 2020, winter of 2020/2021, and summer of 2021, a new network, Richmond Air Monitoring Network (RAMN), of sensors was installed in the City of Richmond, in collaboration with PSE Health Energy and Asian Pacific Environmental Network (APEN). These sensors are designed to measure 2.5 μm particulate matters, nitrogen dioxide, and ozone. The data from three shorter periods over a span of twelve

months were collected to analyze the temporal and seasonal trends of these pollutants.

A third network was installed near Modesto, Stanislaus County Air Monitoring Project, for two-month periods in fall of 2020 and winter of 2020/2021. Eleven ABCDs were installed in parallel with Purple Air PM monitors. Again, these were executed in collaboration with Central California Asthma Collaborative and Valley Improvement Projects.

Data from the Oakland and Richmond sites were most informative. From the Oakland sites, after about 20 to 40 days, most sites reached the 100-day average. This data allowed setting the sampling periods in Richmond and Modesto to 30 days. From the Richmond network, the data showed higher pollutant levels near roadways (Richmond Parkway and Interstate 580) and rail lines, than the communities in the hills, with little seasonal variations. Chelsea also showed that for the Oakland data at one hour resolution, black carbon concentration was the highest during noon hour, as compared to average. From the Modesto network, during the fall fire season, the particulate matter concentration was four times that of fall season with no wildfire. The power of higher resolving power in time and space was demonstrated by the Oakland data; several sites showed elevated levels at midnight, and it was discovered that trucks line up starting at midnight to be first in line when the port opens at 5 am. Additionally, high spatial resolving power provided information on the decrease of black carbon concentration as a function of distance.

Chelsea concluded by stating the importance of local/community measurements of black carbon to support legislative action. However, the efforts to operate and maintain densely distributed sensors are substantial. It was also pointed out that black carbon gradient can sometimes be observed in less than 100 m, therefore, even more densely situated, as well as, indoor sensors were implicated.