Enhancing Analytical Skills and Competencies to Support Industry Research and Development

Leonel M. Santos, Ph.D.
Balik Scientist at De La Salle University

February 3, 2020 – April 7, 2020

Approved Schedule	New Schedule
01 February – 30 April 2020 (90 days)	03 February – 07 April 2020 (65 days)

Nature of Problem

DLSU is setting-up a Central Instrumentation Facility (CIF) located at the Laguna Technopark equipped with advanced instrumentation such as the 600 MHz NMR, LC-MS/MS QToF, HPLC, ICP-MS, CHNS Elemental analyzer, ATR-FTIR, GC-MS, Particle size analyzer, TEM, SEM, FIB, Confocal microscope, among others . The facility will serve the research needs of the university. It is also envisioned to serve the QA and R&D needs of the industry particularly the food, specialty chemicals, and biotech industries. There is a need to set the standards for the various analyses to better serve the requirements of the industry to meet the international specifications. Local expertise may be available but these are usually connected to the industry, if not exclusive to the company. It is necessary to develop and apply the proper procedure for Analytical Instrument Qualifications. This will ensure that all the instruments are suitable for its intended applications. Dr. Santos will support and provide guidance in the instrument qualifications to include the design, installation, operational, and performance. Someone with the international expertise of Dr. Santos can help in setting the facility and in connecting with the appropriate industry players.

Leonel M. Santos, Ph.D.

Dr. Santos is a PCIEERD Balik Scientist hosted by the DLSU Chemistry Department and the Central Instrumentation Facility. He was the former director of the United States Pharmacopeia (USP) who championed the USP monograph modernization and compendial procedure validation through strong collaboration with US-FDA and instrument manufacturers. He also worked as Supervisor of Quality and Regional Analytical Services for Dupont Chemical Solutions Enterprise. Dr. Santos has an extensive record of success in setting standards for commercial products through monograph development, method development and validation, scientific communications, reference standards, quality assurance, compliance, and laboratory research. He has also experiences in impurity analysis for specialty chemicals, agricultural, and biotech products. He obtained his PhD in Analytical Chemistry from the University of Louisville in Kentucky USA and his BS Chemistry degree from UP Diliman.

Daily Schedule of Activities

Days	Where he will be	Notes
Mondays	DLSU Laguna Campus at the Central Instrumentation Facility (CIF)	Dr. Santos takes the 7:30 am shuttle from DLSU Taft and arrives at DLSU Laguna at around 8:30-9:00 am. He takes the 3:30 pm shuttle back to Manila. If he has meetings/consultations at DLSU Taft, he may leave earlier.
Tuesdays	DLSU Laguna Campus at the Central Instrumentation Facility (CIF)	
Wednesdays	DLSU Taft Campus at the Chemistry Department	He is available for consultation with the projects of students and faculty. He has a graduate class at 6:00 - 9:00 pm on Special Topics in Analytical Chemistry at room SJ 113.
Thursdays	DLSU Laguna Campus at the Central Instrumentation Facility (CIF)	Dr. Santos takes the 7:30 am shuttle from DLSU Taft and arrives at DLSU Laguna at around 8:30-9:00 am. He takes the 3:30 pm shuttle back to Manila. If he has meetings/consultations at DLSU Taft, he may leave earlier.
Fridays	DOST ITDI Director's office for engagements with Admatel, OneLab and Standards & Testing Division	We already visited ITDI, Admatel and OneLab and met with the heads (Dr. Annabelle Briones, Dr. Celi Monsada, Dr. Rosalinda Torres). They look forward to the engagement with Dr. Santos every Friday as they would be needing him for the planned expansion of services at Admatel and the proposal on impurity analysis at Onelab/STD.

Terms of Agreement (TOR)

1. Conduct assessment on the DLSU facility to identify gaps in serving the needs of the industry.
2. Facilitate the creation of Standard Operating Protocols in handling analysis following international standards such as the ASTM, AOAC, USP, etc.
3. Conduct seminars and training in Analytical techniques to include industry practitioners, researchers and students.
4. Hold classes in DLSU on Advances in Analytical Techniques to train the next generation of scientists that the industry needs.
5. Lead a team to write a proposal to facilitate academe-government industry partnership through R&D collaboration using CIF facility.
6. Provide technical expertise/consultation on existing projects or proposals.

Summary

Activities (*as indicated in TOR)	Deliverables (*as indicated in TOR)	% accomplished	Remarks
1. Conduct assessment on the DLSU facility to identify gaps in serving the needs of the industry.	Conducted a presentation on **March 2, 2020** at DLSU Central Instrumentation Facility regarding the assessment on gaps in serving the needs of the industry: A. ISO 17025 Certification B. Analytical Instrument Qualification C. GMP, GLP, or ISO 17025	100%	
2. Facilitate the creation of Standard Operating Protocols in handling analysis following international standards such as the ASTM, AOAC, USP, etc.	Provided a template for Central Instrumentation Facility a Standard Operating Procedure template **on February 20, 2020**.	100%	

Summary (contd.)

Activities (*as indicated in TOR)	Deliverables (*as indicated in TOR)	% accomplished	Remarks
3. Conduct seminars and training in Analytical techniques to include industry practitioners, researchers and students.	Conducted one-day seminar on **March 9, 2020** at DLSU to various researchers, faculty, and students from various universities. Presented the following topics: 1. Current Trends in Analytical Chemistry 2. Development of Alternative Procedures in Analytical Sciences 3. The Chemistry and Regulations of Impurity Analysis Conducted a 3-hour seminar on **March 10, 2020** at DLSU Central Instrumentation Facility on Analytical Method Validation	100%	TAAS - I

Summary (contd.)

Activities (*as indicated in TOR)	Deliverables (*as indicated in TOR)	% accomplished	Remarks
	Conducted online seminar on **September 12, 2020** to various researchers, faculty, and students from various universities, industry, and government. The following presentation was to be presented by the BSP Awardee to industry practitioners: 1. Analytical Method Lifecycle Management 2. Development of Alternative Procedures in Analytical Science 3. Validation, Verification, and Transfer of Analytical Procedures Seminar/Workshop on Analysis of Drug Polymorphism using NMR (Same But Not Similar: The Necessity of Analyzing Polymorphism Forms of Drug Product Development and Manufacturing) was conducted **April 30, 2021**.	100%	TAAS – II Webinar/ Workshop

Summary (contd.)

Activities (*as indicated in TOR)	Deliverables (*as indicated in TOR)	% accomplished	Remarks
4. Hold classes in DLSU on Advances in Analytical Techniques to train the next generation of scientists that the industry needs.	▪ Held classes at DLSU on Advances in Analytical Techniques as graduate course (Chem 813 – Special Topics in Analytical Chemistry) every Wednesdays 6:00 PM to 9:00 PM ▪ Five meeting were held until school was closed due to Coronavirus 2019 lockdown. Provided the students the following presentations based on established syllabus: A. Analytical Instrument Qualification B. Basic Concepts of HPLC in Pharmaceutical Analysis C. Basic Concepts of Analytical Electrochemistry D. Analytical Method Development of Pharmaceutical Products E. Guidances on Analytical Method Validation from FDA, ICH and USP F. Validation and Verification of Analytical Procedures ▪ Also provided to each student a “Method Validation Report Package” for them to do an evaluate and submit as report at the end of the class	100%	

Summary (contd.)

Activities (*as indicated in TOR)	Deliverables (*as indicated in TOR)	% accomplished	Remarks
5. Lead a team to write a proposal to facilitate academe-government-industry partnership through R&D collaboration using CIF facility	▪ Provided a proposal to establish a collaboration between academe-government-industry partnership of the analysis of drug substance and drug products polymorphism using solid state NMR and FT-IR instruments at DLSU Central Instrumentation Facility.	100%	
6. Provide technical expertise/consultation on existing projects or proposals	▪ Provided evaluation on two project proposals of DOST Standard Testing Division (STD) 1. Establishment of Testing Facility for the High-speed Analysis of Active Pharmaceutical Ingredients and its Process Impurities 2. Establishment of the Halal Innovation Center for Cosmetics and Toiletries	100%	

Deliverables:

Date	Activity	Expected audience	Proposed venue
February 20, 2020 (Thursday)	**Provided SOP Template for NMR (Nuclear Magnetic Resonance) Instrumentation at Central Instrumentation Facility – DLSU Laguna**	· CIF personnel	CIF, DLSU Laguna
March 2, 2020 (Monday)	**Seminar on Regulations and Regulatory processes for CIF personnel on ISO-GMP-GLP**	· CIF personnel	CIF, DLSU Laguna
March 9, 2020 (Monday)	**Seminar on "Trends and Approaches on Analytical Science"-I (TAAS - 1)** (1) Current Trends in Analytical Chemistry (2) Development of Alternative Procedures in Analytical Sciences (3) The Chemistry and Regulations of Impurity Analysis	· DLSU students & faculty · External academic students and faculty · Industry people	Andrew Gonzales Hall, DLSU Taft

Deliverables:

Date	Activity	Expected audience	Proposed venue
September 12, 2020 (Saturday)	**Seminar on Trends and Approaches on Analytical Sciences-II (TAAS-1I)** (1) Analytical Life Cycle Management, (2) Development of Alternative Procedures in Analytical Sciences, and (3) Validation, Verification, and Transfer of Analytical Procedures	▪ Industry staff ▪ DLSU Faculty and researchers ▪ FDA/DOST personnel ▪ External academic students and faculty	Online Webinar
April 29, 2021 (Thursday)	**Wrote a proposal for an academic, industry, and government collaboration focused on drug quality**.	▪ Industry staff ▪ DLSU Faculty and researchers ▪ FDA/DOST personnel ▪ External academic students and faculty	Online Webinar
April 30, 2021 (Friday)	**Seminar/Workshop on Analysis of Drug Polymorphism using NMR (Same But Not Similar: The Necessity of Analyzing Polymorphism Forms of Drug Product Development and Manufacturing)**	▪ Industry staff ▪ DLSU Faculty and researchers ▪ FDA/DOST personnel ▪ External academic students and faculty	Online Webinar

Significant Contributions:

❖ **Rationale**

1. Initiate collaboration between industry, academia, and government through symposiums and webinar/workshop based on various topics of interests.
2. Develop understanding on establishing quality management systems, development of SOP template, analytical instrument qualification, and ISO certification.
3. Taught Analytical Method Development and Analytical Method Validation as course and at Central Instrumentation Facility.

Significant Contributions:

❖ **Highlights**

1. Presented topics of interest in the field of pharmaceutical analysis, development of quality standards, and regulations attended by more than students, academic faculty, industry practitioners, and government staff.
2. Assisted the DLSU in determining gaps for laboratory certification, drafting SOP, and developing proposal to utilize laboratory instrumentation for strengthening academia-industry-government collaboration in pharmaceutical research and development.
3. Establish an initial plan of future activities with DOST units (ADMATEL and Standards and Testing Division).
4. Reached out to various stakeholders of the importance of quality and collaboration.

Impact of Analytical Chemistry in Ensuring the Quality of Drugs

Food and Drug Administration (US-FDA)

- regulatory approval for - safety, efficacy, and process capability
- once product is approved for sale in public, FDA ensures the quality based on USP standards

United States Pharmacopeia (USP)

- standard setting organization as prescribed in the federal law
- publishes the compendial book describing the quality of drugs
- develop reference standards for use in the analytical methods

5Ps Summary

Presentations made	Title of Presentation	Date	Place
DLSU-CIF	▪ ISO 17025 Certification ▪ Analytical Instrument Qualification ▪ GMP, GLP, or ISO 17025	March 2, 2020	DLSU-CIF
DLSU-CIF	▪ Analytical Method Validation	March 10, 2020	DLSU-CIF
Trends and Approaches on Analytical Science"- I	▪ Current Trends in Analytical Chemistry ▪ Development of Alternative Procedures in Analytical Sciences ▪ The Chemistry and Regulations of Impurity Analysis	March 9, 2020	DLSU-Taft Manila
Trends and Approaches on Analytical Science"- II	▪ Analytical Method Lifecycle Management ▪ Development of Alternative Procedures in Analytical Science ▪ Validation, Verification, and Transfer of Analytical Procedures	September 12, 2020	Online Webinar
Webinar Workshop	▪ Seminar/Workshop on Analysis of Drug Polymorphism using NMR (Same But Not Similar: The Necessity of Analyzing Polymorphism Forms of Drug Product Development and Manufacturing)	April 30, 2021	Online Webinar

Title of Presentation	Significance of the Presentation
ISO 17025 Certification	▪ The **ISO 17025 accreditation** is the most **important** standard for testing and/or calibration laboratories. ▪ It confirms that a particular laboratory is able to produce precise and accurate test results and calibration data, including: Traceability of measurements and calibrations to national standards.
Analytical Instrument Qualification	▪ By qualifying the used **analytical instruments**, we can ensure that active ingredients and finished pharmaceutical products are analyzed according to specifications. ▪ In addition, procedures that prove **instrument** accuracy and repeatability are a must.
GMP, GLP, or ISO 17025	▪ **GMP** (**Good Manufacturing Practice)** is a quality control system which makes sure that every pharmaceutical product is adequately tested and dosed for optimal effectiveness. ▪ **GLP** (**Good Laboratory Practice**) helps to ensure the credibility and traceability of data submitted, thereby addressing the issue of **non**-reproducibility in many biopharmaceutical experiments.
Analytical Method Validation	▪ **Validation** of **analytical** test **methods** is **important** for every stage of the drug development life cycle. ▪ **Methods** must be shown to be acceptable for their intended use and must provide accurate and reliable results at every stage of development, from pre-clinical trials through approved and marketed product

Trends and Approaches on Analytical Science”- I

Trends and Approaches in Analytical Science (TAAS-1)

A whole-day lecture on the advances in Analytical Chemistry

March 9, 2020 | 8:30 AM – 5:00 PM | Y407-Y409, Yuchengco Hall, DLSU Manila

P R O G R A M M E

08:00-08:30 Registration

08:30-09:00 National Anthem & Doxology

Opening Remarks *Dr. Jaime Raul Janairo (Chair, Chemistry Dept.)*

09:00 – 10:30 Current Trends in Analytical Chemistry *Dr. Leonel Santos (Balik Scientist DOST-PCIEERD)*

10:45 – 12:00 Development of Alternative Procedures in Analytical Science *Dr. Leonel Santos*

12:00 – 13:00 L U N C H

13:00 – 14:00 The Chemistry and Regulations of Impurity Analysis *Dr. Leonel Santos*

14:00 – 17:00 Capabilities & Research Prospects of Analytical Instruments at DLSU Laguna

1. Gas Chromatography (GC-MS with headspace) – *Christine Ramos (DKSH)*
2. Liquid Chromatography (LC-MS/MS QToF, GPC, HPLC) – *Eillen Valeri Cruz (DKSH)*
3. Column Chemistry – *Christian dela Cruz (DKSH)*
4. Dynamic Light Scattering with zeta sizer and rheometer – *Andressa San Gabriel (DKSH)*
5. Inductively Coupled Plasma-Mass Spectroscopy (ICP-MS) – *Franco Singson (Shimadzu)*
6. UV-Vis with reflectance – *Franco Singson (Shimadzu)*
7. Nuclear Magnetic Resonance (NMR) Spectrometry – *Dr. Virgilio Ebajo (DLSU-CIF)*

17:00 – 17:15 Closing Remarks *Dr. Drexel Camacho (Scientific Director, CIF)*

Title of Presentation	Significance of the Presentation
Current Trends in Analytical Chemistry	▪ Explained the principles of pharmaceutical regulatory and compendial regulations ▪ Presented Case Study on Acetaminophen or Paracetamol - Organic Impurity Analysis ▪ Discussed the Case Study on Acetaminophen or Paracetamol in terms of Elemental Impurities and Residual Solvent Analysis ▪ Described a Case Study on the product contamination of Dextromethorphan ▪ Explained the impact on Drug Quality Standards on Identification, Assay, Organic Impurities, Tests
Development of Alternative Procedures in Analytical Sciences	▪ The development of alternative procedures for Residual Solvents and Elemental Impurities when the compendial procedures are problematic was presented. ▪ The process of using USP methods or procedures was discussed, including ways to resolve issues or difficulties in sample analyses. ▪ A discussion on system suitability adjustments and sample preparation will be discussed.
The Chemistry and Regulations of Impurity Analysis	▪ A presentation regarding the classification, formation and analysis of impurities in pharmaceutical products was explained and presented. ▪ The significant impact of impurities on the quality of drug substances and drug products was described in details. ▪ Guidelines on Impurities based on US-FDA, ICH, and USP was presented.

Trends and Approaches in Analytical Sciences II

A Free Webinar hosted by the De La Salle University Central Instrumentation Facility
September 12, 2020 7:00 PM PST

RESOURCE SPEAKER

Leonel Santos, Ph.D.

Balik-Scientist, DOST-PCIEERD

Former Director of Chemical Medicines, United States Pharmacopeia (USP)

Former Analytical Standards Supervisor, Du Pont Agricultural Products

Topics

01 Analytical Method Life Cycle Management

02 Development of Alternative Procedures in Analytical Sciences

03 Validation, Verification, and Transfer of Analytical Procedures

Platforms

Main Session via Google Meet

Live Streaming via

https://rb.gy/uf3m7z

https://rb.gy/yv2hg8

#TAAS2
#DLSUCIF

Title of Presentation	Significance of the Presentation
Analytical Method Lifecycle Management	▪ A new proposed new USP General Chapter <1220> was presented and explained to prepare pharmaceutical industry of future changes in establishing the quality of drugs. ▪ The current processes involving compendial management was also presented. ▪ Then the goals of the new general chapter in terms of addressing the described challenges was explained and focusing on the continuous process of lifecycle management. ▪ Some specific examples of what may be included in the USP monographs as a result of this new proposed general chapter was also presented.
Development of Alternative Procedures in Analytical Science	▪ The development of alternative procedures for Residual Solvents and Elemental Impurities when the compendial procedures are problematic was presented. ▪ The process of using USP methods or procedures was discussed, including ways to resolve issues or difficulties in sample analyses. ▪ A discussion on system suitability adjustments and sample preparation will be discussed.
Validation, Verification, and Transfer of Analytical Procedures	▪ The validation, verification, and transfer of analytical procedures as the main tool in pharmaceutical analysis were explained. ▪ Discussion on the analytical performance characteristics as the basis of method validation, different categories of methods, and robustness was presented. ▪ The principles of verification of analytical procedure was shown followed by specific case studies.

Seminar/Workshop on Analysis of Drug Polymorphism using NMR (Same But Not Similar: The Necessity of Analyzing Polymorphism Forms of Drug Product Development and Manufacturing)

Title of Presentation	Significance of the Presentation
Seminar/Workshop on Analysis of Drug Polymorphism using NMR (Same But Not Similar: The Necessity of Analyzing Polymorphism Forms of Drug Product Development and Manufacturing)	▪ The polymorphism of drug substances and drug products was presented to describe how it affects the quality, safety, and efficacy of pharmaceutical products. ▪ The formation of polymorphs in drug substances and drug products affecting the physiochemical properties during formulation development and manufacturing was described in the presentation. ▪ Various analytical method of polymorph analysis was discussed. The principle and application of solid-state NMR in polymorph analysis was presentation in the program. ▪ Regulatory guidelines based on US-FDA, WHO, EMA (European Medicines Agency), and ICH (International Conference on Harmonization) was presented and explained including the impact of polymorphism in bioavailability, bioequivalence, and stability. ▪ Example monographs related to controlling and defining the quality of drugs in the presence of polymorphs were shown. ▪ The presentation provide examples and impact of polymorphism in the quality of drug substances and drug products.

5Ps Summary

	Name	Duration	Place (if applicable)
People Trained	Cristian Argamino	27 days	DLSU-CIF
	Alona Intac	27 days	DLSU-CIF
	Dr. Virgilio Ebajo	10 days	DLSU-CIF
	Jonathan Daved dela Cruz	5 days	DLSU-Taft Manila
	Jianne Manalo Gabriel	5 days	DLSU-Taft Manila
	Leah Adaya Gamban	5 days	DLSU-Taft Manila
	Anlee Allado Refuerzo	5 days	DLSU-Taft Manila
	Jayvee D Tabal	2 days	DOST-ADMATEL
	Lynne Jerisa Alfeche	2 days	DOST-ADMATEL
	Clairezelle Cruz	2 days	DOST-ADMATEL
	Zamantha Martin	2 days	DOST-ADMATEL
	April Joy Haro	2 days	DOST-ADMATEL
	Isaiah E Ubando	1 day	DOST-STD
	Vernalyn R Abarintos	1 day	DOST-STD

Challenges

1. Coronavirus -19 ECQ lockdown in Metro Manila
2. Difficulty in communicating with pharmaceutical industry in terms of contact person and phone number/email address.
3. Difficulty in obtaining response from Philippine FDA on interest in collaborating with academia and industry.

Recommendations

1. Follow up with pharmaceutical colleges and some pharmaceutical industry in their interest in having an international conference.
2. Strengthen the collaboration and working relationship between the pharmaceutical industry, instrument manufacturers, pharmaceutical colleges, and Philippine FDA through common beneficial projects of interests.
3. Develop Drug Reference Standards and update the Philippine Pharmacopeia.
4. Organize training (webinars or face to face) between pharmaceutical stakeholders.

Recommendation to Develop DLSU – CIF Polymorph and Crystallization Screening Laboratory

- **The development of DLSU – CIF Polymorph and Crystallization Screening Laboratory will primarily perform polymorphism analysis in drug substances (active pharmaceutical ingredients) and drug products (finished dosage forms).**
- **DLSU – CIF Polymorph and Crystallization Screening Laboratory will utilize the Solid State NMR as primary instrument in polymorphism analysis and use FTIR-ATR as supporting and confirmatory method.**
- **Collaborate with Government (FDA), academia, and industry in Polymorph and Crystallization studies**

Proposal to Develop DLSU – CIF Polymorph and Crystallization Screening Laboratory

- **Applications of polymorph and crystallization screening laboratory are:**
  - **Determine the drug substance polymorphic form between RDL (reference listed drug) against generic drug**
  - **Support discovery, synthesis, scale-up, and formulation development of pharmaceutical solid dosage forms to pharmaceutical industry**
  - **Develop high throughput screening system for polymorphic analysis**
  - **Provide analytical support on polymorphism study in academia**
  - **Establish database of enantiotropic relationship between polymorphs**
  - **Secure intellectual property for polymorphic forms**
  - **Develop application of polymorphic analysis in other industrial materials such as solar panels, etc.**

Thank You

Questions?