Canna-Pharma 2019
Advancing the Science of Medicinal Cannabis Through
GMP, Quality Control, & Regulatory Compliance
November 13–14, 2019, Marriott Mission Valley, San Diego CA

Featuring Lessons Learned and Case Studies from Industry Experts:

With Comprehensive Coverage On:

- Challenges in Creating Standards for Quality Control of Cannabis Derived Products
- Updates from Industry Working Groups: ASTM D37, AHPA, USP, & AOAC International
- Analytical Testing Strategies for Pesticides, Trace Metals & Other Contaminants
- Regulatory Panel Discussion—Hear from the Experts
- Cannabis Genetics: The Path to Better Medicinal Cannabis
- Hot Topics in Therapeutic Cannabis Research
- Key Formulation Considerations for Improved Bioavailability of Cannabinoids
- Evaluating the Volatile Constituents of Different Cannabis Varieties using Various Sample Preparation Approaches, and Mass Spec Detection
- Environmental Monitoring for GMP Compliance in Grow Facilities
- Cannabis Microbiome Sequencing: Implications for Cannabis Safety Testing
- Cleaning Validation and GMPs for Medicinal Cannabis Products
- The Therapeutic Potential of Cannabinoid Medicines Applied on the Skin
- Intellectual Property Considerations for Medical Cannabis
- And Much More!

With Representation From:

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- AHPA
- Gattefossé
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- ICCI
- University of Maryland
- STERIS
- Alconox
- MEDICAL GENOMICS
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- SepSolve Analytical
- VegAS Analytical Services
- Colorado Department of Public Health & Environment
- MMCC
- California Department of Public Health
- PharmaEd Resources Inc.
Wednesday, November 13

7:45  Registration & Complimentary Breakfast

8:20  Opening Remarks from Chairperson

8:30  Developing Normative Standards at ASTM International

Dr. Ralph M. Paroli, Director, R&D, National Research Council of Canada and Robert J. Morgan, Director, ASTM International

Standard developing organizations (SDOs) such as ASTM International develop product safety standards using the consensus process. This, of course, gives everyone an equal voice in the process. The purpose of these voluntary standards is to help enhance safety and performance. The standards help enhance safety because it provides regulators with tools to develop laws and regulations to ensure that the products we are consuming are tested or analyzed with confidence using methods which have appropriate certification, calibration, etc. For example, pesticide presence needs to be measured accurately so that the levels allowed by regulators are within the appropriate tolerances. This presentation will provide an update on what has been accomplished at ASTM International Committee D37 in the areas of: Indoor and Outdoor Horticulture and Agriculture; Quality Management Systems; Laboratory; Processing and Handling; Security and Transportation; Personnel Training; Assessment, Credentialing; and Industrial Hemp.

9:00  Challenges in Creating Standards for Quality Control of Cannabis Derived Products

Holly E. Johnson, Ph.D., Chief Science Officer, American Herbal Products Association, & Member, USP Expert Panel on Medical Cannabis

Cannabis derived natural products for oral delivery, especially medicinal preparations and dietary supplements, are steadily gaining popularity with consumers and practitioners. While there is some optimism about the current efforts to clarify the legal status of some such products in the US, the pervading legal and regulatory uncertainty has led to technical challenges in assuring product quality. The proliferation of an enormous variety of delivery vehicles in the market also presents challenges in matrix extension validation for standard test methods. This talk will discuss initiatives to create useful and rigorous quality standards for industry, including the United States Pharmacopeia’s Expert Panel on Medical Cannabis and AOAC’s Cannabis Analytical Science

9:30  In a rapidly changing industry, regulatory bodies, product manufactures, and scientists strive to provide cannabis consumers with safe products with known concentrations of constituents of interest. Although cannabis cultivators and product manufacturers may conduct in-house testing to ascertain the status of product development, all parties look to the external third-party testing labs to provide empirical data that attests to the veracity of the statements made about the final product.

These third-party analytical testing laboratories must rely on solid scientific processes and technologies to yield sound results accurately and precisely. Relying on laboratory accreditation to the pinnacle international standard of laboratory quality that is ISO/IEC 17025, laboratories are compelled to develop analytical test methods that are based using appropriate technology and competence to build methods that are well characterized to a number of parameters as well as forming a determination of measurement uncertainties.

This session will discuss progress chemists have made to the development of standard test methods with the assistance of international scientific organizations. Specifically, participants will leave with a list of test methods validated analytical methods that are applicable to a number of parameters as well as forming a determination of measurement uncertainties.

10:00  Quality Control & Analytical Testing: Achieving Standardization

Moderator: Chair Wayne Nasby

Panelists: Ralph Paroli, Holly Johnson, Susan Audino

Participants: The Audience

10:30  Morning Coffee & Networking Break

10:55  The Challenges of Regulatory Compliance in a Fragmented Landscape

Heather Despres, Director of Patient Focused Certification, Americans for Safe Access

In 1996 California became the first state to allow the use of medical marijuana. Products went largely unregulated and untested until 2015 when the Medical Cannabis Regulation and Safety Act was passed. This Act created the regulatory framework for cannabis businesses and initiated mandatory testing of finished products. This framework
was then utilized when the Adult Use of Marijuana Act passed in 2016 and both adult-use and medical regulations were combined into the Medical and Adult-Use Cannabis Regulation and Safety Act was passed in 2017.

This presentation will discuss the current changes in California state regulations and provide information on how becoming certified through third-party assessment and certification programs can help businesses weather the seemingly constant changes in regulations. By comparing and contrasting California regulations with other state regulations we will see how different regulations can be between jurisdictions and how compliance certification companies must stay on top of all these changes to ensure continued compliance.

**Keynote Address: Cannabis Product Ingredients: What Interlocking Regulatory Boundaries Make Sense?**

**Dr. Brad Douglass, VP of Regulatory Affairs, The Werc Shop, & Dr. Jeffrey C. Raber, CEO, The Werc Shop**

There is an old FDA axiom that summarizes when a substance is a drug and/or a food, if it can potentially be both: “First a food, always a food. First a drug, never a food.” Such gating details and the compositional definitions of food, dietary supplements, and drugs are instructive to those interested in any cannabis-derived or -inspired products. The reasons are manifold including likely draft U.S. hemp regulations and, perhaps in the foreseeable future, U.S. federal adult-use marijuana product regulation. We will synthesize the relevant regulatory doctrine before providing a potential road-map for incorporating all cannabis products into the existing landscape while highlighting the role analytical chemistry has to play. Importantly, we will describe why this issue must be collaboratively addressed by all stakeholders—including hemp, marijuana, and pharma—if we hope to succeed any time soon.

**Lunch Break**

**Q & A—Ask the Regulators**

**Regulatory Panel: The Present & Future of Medicinal Cannabis Regulation**

**Moderator: Chair Wayne Nasby**

Presenters/Panelists:
- Zarha Ruiz, Chief of Inspection & Compliance, Manufactured Cannabis Safety Branch, California Department of Public Health
- Lori Dodson, Deputy Director, Maryland Medical Cannabis Commission
- Heather Krug, State Marijuana Laboratory Sciences Program Manager, Colorado Department of Public Health and Environment

Participants: The Audience

**Research Spotlight—New Sample Preparation Techniques**

**Comprehensive Chromatography of Terpenes and Terpenoids from Cannabis Samples: Modernizing the Process from Sample Preparation Through to Data Analysis**

**Matthew Edwards, Business Development Manager, SepSolve Analytical, partnered with Markes International**

The classification of terpenes and terpenoids is an important aspect of cannabis analysis. This is due to the distinctive aroma and flavour that they impart, as well as their contributions to physiological effects and psychoactivity. Specific terpene profiles can be engineered by plant breeders in order to give the desired therapeutic effects.

Volatile organic profiling of cannabis samples often requires extensive sample preparation for efficient extraction and concentration the target analytes. Conventional sample introduction/injection techniques for GC–FID or GC–MS can result in the abundance of important terpenes being over-estimated, due to the co-elution of similar compounds or oxygenated derivatives resulting in reduced confidence in data quality.

This study demonstrates the improved performance of conventional techniques (e.g. Headspace and SPME) using trap-based focusing technology (Headspace-trap and SPME-trap). Appropriate sample preparation coupled with two-dimensional gas chromatography with time-of-flight mass spectrometry (GC×GC-TOF MS) provides a powerful analytical approach to cannabis analysis. This enhanced analytical performance allows common co-elutions to be resolved for increased confidence in cannabis chemistry and more robust profiling of terpenes across different cannabis strains.

**Afternoon Networking Break**

**Evaluating the Volatile Constituents of Different Cannabis Strains using Various Sample Preparation Approaches, and Mass Spectrometric Detection**

**Gyorgy Vas Ph.D., VasAnalytical, Flemington, NJ**

The legalization of medicinal and recreational marijuana in North America requires an urgent need for reliable, accurate and economical analytical methods to control the active and other constituents of the cannabis plant. In addition to the natural constituents of the plants, trace level contaminants also need to be rigorously controlled.

Cannabis plants and the derived oils contain more than 100 different terpenoids. Terpenes are one of the most abundant class of compounds naturally present in the cannabis plant, and some believe they have therapeutic
Cannabis, Keeping it Clean

Beth Kroeger, Technical Services Manager, STERIS

As cannabis use becomes more mainstream, there is a growing demand for testing to ensure the safety of not only medical marijuana, but recreational cannabis as well. Both in Canada and the US, strict guidelines have been imposed on the industry to ensure the final product does not contain significant levels of harmful substances. This presentation will provide an overview of the industry from cultivation, harvesting, and extraction along with the industry issues for meeting these requirements at each of these stages.

Critical Cleaning—The Key to Quality & Safety

Michael Moussourakis, Senior Director, Strategic Affairs, Alconox Inc.

Critically clean processing equipment, whether it be labware, glassware, instrumentation, or processing and extraction equipment, is vital. The potency, purity and quality, essential characteristics of any drug, rely on critically clean surfaces. Cannabis is no different, and in fact, likely more difficult than traditional drug manufacturing. Waxy, resin, oily and sticky residues abound which can be highly adherent, difficult to emulsify, and just a plain challenge to remove. Strong solvents and harsh chemicals might be a quick answer, for sure. But the wise answer, the innovative answer, are detergents that are not only effective, but end-user safe, aqueous, free-rinsing, interfering residue-free, biodegradable, and without any added dyes, fragrances, brighteners or softeners. In other words, maintaining the whole reason why cannabis, and its “natural” state is sought after.

Critical cleaning is defined as when the level of cleaning directly impacts the value of the final product. The cannabis and related industries certainly apply, and mastery of both the right detergents, for the right applications, right procedures, and right guidance documentation, ensures the end product is at its highest efficacy possible.

End of Day One

Thursday, November 14

Complimentary Breakfast

Research Spotlight—Unlocking the Therapeutic Potential of Cannabis Derived Compounds

Ethan Russo, M.D., Director of Research and Development, International Cannabis and Cannabinoids Institute, Prague

Cannabis has acquired a public reputation as a miracle drug that has not yet been supported by randomized clinical trials. However, it has proven extremely versatile in treatment in a wide variety of otherwise recalcitrant disorders through modulation of the endocannabinoid system (ECS). This presentation will focus on the scientific rationale from basic science research, available clinical data, and prospective formulation of cannabis-based medicines to treat brain tumors, Alzheimer disease, traumatic brain injury (post-concussion syndrome and chronic traumatic encephalopathy), and endometriosis, all disorders where “conventional medicine” has failed to produce acceptable results.

Cannabis-Based Drug Delivery: University Lab to Clinical Trials

Dr. Audra Stinchcomb, Professor, University of Maryland & Founder, F6 Pharma, Inc.

Topical, transdermal, and oromucosal dosage form development will be discussed. Primary research focus areas will include microneedle-enhanced delivery and translational research models for public-private partnerships. Currently Dr. Stinchcomb is focusing significant effort in concert with the FDA on the evaluation of multiple dermal dosage forms in human subjects, with the end goal of creating validated in vitro-in vivo correlation studies that may help to improve the efficiency and cost of the drug development process. The research group is also developing the best way to formulate and evaluate drug delivery from oromucosal systems in vitro.
As interest in Cannabis grows, identifying genes and gene networks involved in production of the desired metabolites (cannabinoids and terpenes) as well as networks necessary to optimize cultivation potential, will become increasingly important as demand for specific metabolites or cultivars grows. In addition to the work Steep Hill has done identifying and analyzing cannabinoid and terpene genes, we have also started a systematic analysis of upstream genes in the cannabinoid and terpene metabolic networks, and genes related to growth, development and oil production. Recent advances in reference to genome availability have allowed us to identify and map novel genes and begin the process of metabolic network annotation and SNP identification. SNPs identified in the genes of interest are screened using a panel of known cultivars to identify any potential informative regions associated with one or more SNPs. Informative regions are then further assessed for their level of informativeness by comparison to chemical or other phenotypic data where available. The combined process contributes to a database that, using the correct methodology, provides a proxy for sequence information, and where applicable, functional outcome. This information can be used to screen for new cultivars, or breed for specific cultivars of medical importance.

GBS uses a novel, whole plant approach to discovering proprietary formulations of cannabis-derived compounds that show promise for the treatment of specific diseases. GBS has focused its efforts on finding therapies for patient groups that are largely underserved, and they are using novel delivery methods to ensure bioavailability and to provide time-released versions of their patent-pending, cannabinoid-containing complex mixtures (CCCM™).

Although many cannabis researchers and biopharma companies have focused on the activities of single cannabinoids, GBS leverages powerful molecular synergies derived from whole plant extracts that are then further-refined and standardized. Most other cannabis-based biopharmaceutical companies are studying one of the two most abundant cannabinoids in the plant, either tetrahydrocannabinol (THC) or cannabidiol (CBD); whereas, GBS embraces naturally occurring mixtures of approximately 480 bioactive compounds in the cannabis plant. GBS has demonstrated correlations between extracts from different “chemovars”, chemical variations of the cannabis plant, and potential therapeutic efficacy for different specific human diseases.

Our drug discovery process combines: 1) high throughput screening of tens of thousands of combinations of compounds derived from specific chemovars of the cannabis plant in well-established cellular models of diseases and 2) a proprietary network pharmacology algorithm for the prediction of complex therapeutic mixtures. By carefully screening the contributions of the individual compounds within our disease-specific chemovars, we discovered our patent-pending CCCM™ for the treatment of neurodegenerative disorders, inflammatory disorders, cardiovascular disorders, and chronic/neuropathic pain.

With the looming ease of regulations around the globe, there is an expressed need for adequately dosed, age appropriate cannabinoid medicines. The window of opportunities for new cannabinoid drugs currently includes the treatment of multiple sclerosis, seizures, neuropathic/intractable pain in cancer patients, and nausea. There are also indications for anti-inflammatory effect, psychotherapy, and rehabilitation from opioid addiction.

Meanwhile, studies show that only 3-8% of orally administered cannabinoids reach the systemic circulation. This poor bioavailability is in part attributed to the poor gastrointestinal (GI) solubility of these compounds resulting in erratic and variable absorption from the GI tract. Additionally, cannabinoids undergo a significant first pass metabolism in the liver following GI absorption. These properties render cannabinoids as excellent candidates for Lipid-Based Drug Delivery (LBDD). This presentation discusses the key considerations for enhancing the delivery of cannabinoids, focusing on LBDD for immediate or sustained action.

Due to its wide variety of medical benefits, cannabinoids are used to treat a number of common conditions, including chronic pain, inflammation, seizures, insomnia, spasms, multiple sclerosis, and mental disorders such as anxiety and depression. As the topical products, medical cannabinoids could be directly applied to certain areas of the body as an effective means of relieving pain and soreness, reducing inflammation, and soothing inflammatory skin conditions such as psoriasis, dermatitis, and eczema.
For each pathology, it remains to be determined what type of cannabinoid and what route of administration are the most suitable to maximize the beneficial effects of each preparation and minimize the incidence of undesirable reactions.

Due to low bioavailability of oral cannabinoids formulations, alternative routes of drug administration, including mucosal or sublingual dosing, vaporization of product and inhalation, and rectal administration, have been developed to improve the amount of delivered cannabinoids.

The transcutaneous is another alternative route of cannabinoid exposure that avoids first-pass metabolism and improves bioavailability. Also, transdermal delivery of cannabinoids is hoped to reduce negative side effects seen with inhalation or oral dosing products.

The main aim of our study was to evaluate In Vitro percutaneous absorption profiles of major (THC/CBD) alone, and in combination with minor cannabinoids onto and through human ex vivo skin dosing with varieties of exclusively developed topical formulations. Specifically, we aimed to compare and evaluate (24/48hrs) In Vitro absorption profiles of the selected cannabinoids in enhance of In Vivo bioavailability. We also expected that the THC induced changes might be more pronounced after oral administration because of the expected presence of the potent psychoactive metabolite 11-OH-THC that could not be formed at all through the skin permeation. Finally, since THC and CBD are chemically related compounds, it has been reported that under certain (acidic) conditions, CBD can be cycled to THC in vitro. More recently the important question has been raised as to whether CBD and THC can also be converted to THC in vivo. Therefore our aim was to ascertain whether permeation CBD through the skin could result in the presence of THC and if so, this could potentially mediate therapeutic effects.

The collected samples analyzed on contents of cannabinoids by UPLC-MS/MS, In addition, the identification of minor cannabinoids and metabolites was achieved by means of UPLC-QToF. In vitro skin absorption, kinetic parameters obtained from both finite and infinite dose model have been calculated and assessed for characterization of topical formulations.

Afternoon Networking Break

Complying with European Union (EU) Requirements for CBD and Medicinal Cannabis Producers to Gain EU Market Access

Jan Zorgdrager, Managing Consultant CMC Development and Manufacturing at the ProPharma Group

In Europe, there is a growing market for medicinal cannabis as well as for CBD and more and more material will be required to satisfy the market. Suppose, you are considering to enter this market. How would you approach that? What would be your strategy, what would be your products to sell and which requirements do you need to fulfill? My presentation will provide answers to these questions. It will include an overview of the legal status in the various EU-countries and discuss the EU-regulations on quality and regulatory aspects. Moreover, it will discuss good distribution practice including im- and export licenses. Also, technical aspects of growing, extracting and isolating of materials will be alluded to. Finally, an overview of clinical studies on Cannabis in Europe will be provided. In short: an update on the challenges and opportunities regarding cannabis in Europe.

Research Spotlight—New Analytical Approaches to Cannabis Safety & Testing

3:00 Tackling Pesticide Analysis in Cannabis: The Analytical Suitability of a Multi-Platform Approach

Dr. Anthony Macherone, Senior Scientist & Strategic Program Manager, Agilent & The Johns Hopkins University School of Medicine

Residual pesticide analyses in cannabis matrices is complicated because of matrix effects and target analytes like pentachloronitrobenzene (PCNB) that are not amenable to common techniques using electrospray ionization (ESI). To overcome this issue, it has been suggested to use negative atmospheric pressure chemical ionization liquid chromatography-tandem mass spectrometry (Ni-APCI LC-MS/MS) for PCNB with a precursor ion of 275.5 m/z. However, a laboratory must consider selectivity as much as sensitivity in the application of a certain analytical methodology and in this case, the ionization mechanism is reported as the loss of HCl followed by formation of an ammonium ion adduct. There are two intrinsic problems with this description 1) the empirical formula for PCNB is C6C15NO2 thus there is no hydrogen atom to lose as HCl, and 2) the formation of a positively charged ammonium ion in negative ionization mode is improbable. In this presentation we prove the correct ionization mechanism for PCNB using Ni-APCI LC-time-of-flight mass spectrometry (Ni-APCI LC-QToF) and evaluate the appropriateness of this analytical technique for PCNB in terms of selectivity, sensitivity, and the fit of the coefficient of determination compared to GC-MS/MS methodologies.

3:35 Cannabis Microbiome Sequencing: Implications for Cannabis Safety Testing

Kyle Boyar, Field Applications Scientist, Medicinal Genomics

The cannabis plant and cannabis products are highly varied and complex matrices. In the absence of rigorous study this immature industry has decided to adopt methods commonly used in food testing to obtain information about the potential microbial hazards present. However, DNA sequencing of both the cannabis microbiome and the conditions before and after culturing tell a tale of inaccurate methodology. Methods that are currently being employed are leading the cannabis industry
astray while blinding them to the real hazards that could be present. This presentation will walk you through the data that shows this and the discoveries we’ve made along the way that will hopefully open discussions for a fresh new perspective on how to tackle microbiological contaminants in cannabis.

**Intellectual Property Munchies In Canna-Pharma**

**Parithosh Tungaturthi, Ph.D., J.D., Registered Patent Agent & Founder, LexKannabis, LLC**

Medicinal cannabis has been gaining increasing popularity over the last few years, in the United States as well as many countries around the world. Cannabis garnered much attention for its potential in the treatment of chronic pain, Crohn’s disease, sickness related to cancer medication, and many other conditions. The use and acceptance of cannabis therapy resulted in multiple new market entrants, including small biotech companies to large pharmaceutical enterprises. Significant financial investment is likely to be in the books for many companies in producing and/or identifying a product that can be commercialized. A return on such investment can only be ensured by properly formulating and executing a—preferably global—strategy to protect the companies’ IP assets. Therefore, as the medical cannabis industry continues its upward trajectory, it is not only important—but essential—for companies to effectively secure its IP in order to gain and maintain a competitive edge.

IP rights can prove to be vital components of success, especially in an emerging market such as medical cannabis. Given the complicated history of cannabis/marijuana legalization, there are many intricacies that the industry leaders must understand regarding securing rights around their technology. The potential problems that may occur when IP rights are ignored should not be overlooked, for the results can mean the difference between success and failure for a business. This presentation provides an overview of IP strategies for protection of medical cannabis-related inventions, including protection of cannabis strains and related plants.

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