PharmaED RESOURCES, Inc.

# Canna Pharma 2023

## Cannabinoid-derived Pharmaceutical Summit

## June 20-21, 2023, Philadelphia, PA

## *Featuring Lessons Learned and Case Studies from Industry Experts*

**Nandu Sarma**
*USP*

**Aurélia DePauw**
*Tetra Bio-Pharma*

**Karolina Urban**
*Avicanna*

**Malgorzata Meunier**
*HAPA Pharm*

**Staci Gruber**
*Harvard Medical School*

**Hunter Land**
*Biopharmaceutical Research Co.*

**Bruce Mackler**
*Ethicann Pharmaceuticals*

**Marilyn Barrett**
*Pharmacognosy Consulting*

**Mandip Sachdeva**
*Florida A&M*

**Terry O'Regan**
*Brains Bioceutical*

**Akeem Gardner**
*Canurta*

**Inayet Ellis**
*Gattefossé*

**Heath Miller**
*Antares Health Products*

**Joseph Grzyb**
*Groff NA*

**Michael Moussourakis**
*Alconox*

**Dijana Hadziselimovic**
*STERIS*

## *With Comprehensive Coverage On:*

- Using Observational Data to Inform Cannabinoid-Based Clinical Trials
- Federally-legal Cannabis: New DEA Policies, New Opportunities for Research and Pharmaceutical Development
- Medicinal Cannabis in Europe: A Review of the Different Medicinal Cannabis Products and the Respective Regulatory Frameworks in European Countries
- Overcoming Formulation & Bioavailability Challenges of Cannabinoids
- Novel Cannabinoids for the Potential Treatment of Traumatic Brain Injury and Neurodegenerative Disorders
- Topical Delivery Formats of Cannabinoids for Dermatological Conditions and Musculoskeletal Pain and Inflammation
- Role of Cannabidiol-loaded Exosomes in TNBC and Chemotherapy-induced Peripheral Neuropathy
- Development of a Synthetic CB2R Agonist as an Immunomodulator to Treat Hyperinflammation
- Lipid-based Formulations for Oral and Topical Delivery of Cannabinoids
- The Cannabis Entourage Effect: A Dive for Scientific Truth
- Critical Considerations for Emulsified Cannabinoid Formulations
- Best Practices for Ensuring Patient & Consumer Safety in Cannabis and Cannabinoid-derived Pharmaceutical Products
- Critical Cleaning—the Key to your Product's Quality & Safety

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## Tuesday, June 20

**7:30** *Check-in & Complimentary Breakfast*

**8:25** 

*Chairperson Michael Moussourakis' Welcome & Opening Remarks*

## *Regulatory Spotlight on US and Europe: Current Problems, Possibilities, & Potential Solutions*

**8:30**

### Federally Legal Cannabis: New DEA Policies, New Opportunities for Research and Pharmaceutical Development

*Joseph Grzyb, CEO, Groff North America*

For over 50 years, the US federal cannabis policy was essentially frozen in place. While individual states pursued various forms of legalization, a limited supply of federally legal cannabis was available only through the University of Mississippi, and then only available to researchers with DEA Schedule 1 registrations. That situation changed in May 2021, with the DEA authorizing four new companies to cultivate and extract cannabis. With consistent, high-quality, high-THC, federally legal cannabis flower and extracts now available, federally funded and privately funded medicinal cannabis research is expanding rapidly. In this presentation, I'll describe the DEA's expansion of cannabis grow and processing registrations, its structure, its benefits and how it supports pharmaceutical development from beginning to end. I'll discuss how the program:

- Expands the availability of high-quality, high-THC, federally legal cannabis flower for extracts and patient dose formulations.
- Enables improved research, better clinical data, and a more science-driven assessment of the benefits of cannabis-based therapies.
- Allows for federally sanctioned cannabis clinical trials nationwide.
- Enables cannabis-based medicines to be put on a path to FDA approval as a botanical drug.
- Unlocks the future potential for cannabis-based medicines to be covered by insurance.

**9:10**

### Creating Nationwide Standards for Quality Control of Cannabis Derived Products: A USP Perspective

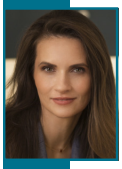
*Nandukumara Sarma, PhD, Director, Dietary Supplements & Herbal Medicines, US Pharmacopeia*

Abstract coming soon

**9:50** *Morning Networking Break*

**10:20**

### Medicinal Cannabis in Europe: What's Really Going On? A Review of the Different Medicinal Cannabis Products and the Respective Regulatory Frameworks in European Countries



*Dr. Malgorzata (Gosia) Meunier, Chief Strategy Officer, HAPA pharm*

After a long period of prohibition, European health institutions have realized the need to regulate patient access to medical cannabis. However, due to regulatory differences in the perception of "what is medical cannabis," Europe is still not facilitating finished pharmaceutical products registered under the MA. The purpose of this presentation is to provide an overview of the regulations in the main European countries where medical cannabis products are available on the market. Compounding as a means of providing patients with access to medical cannabis (in Germany and Poland) will also be discussed.

**11:10**

### Perspective on Developing New Cannabinoid Therapeutic Drugs

*Bruce Mackler, Executive Vice President of Regulatory & Clinical Affairs and Co-Founder, Ethicann Pharmaceuticals*

Developing ethical cannabinoid drugs under FDA allows you to choose two regulatory pathways, either as a botanical drug or as a new pharmaceutical drug. The choice is based on what molecular cannabinoids are used and how pure they are—botanicals are complex mixtures versus drugs are highly purified compounds. Developing a botanical cannabinoid drug has manufacturing, safety and clinical challenges, versus developing a new drug. This presentation reviews botanical drug development versus a new drug, to treat PTSD. Botanical drugs are impure complex mixtures; whereas, new drugs contain highly purified active pharmaceutical ingredients (APIs). Both have safety concerns from their non-pharmacologically impurities, presenting safety challenges. Obviously, THC and CBD, which are approved as drugs, are easier; whereas, choosing delta 8-THC, CBG, CBN, or other unapproved cannabinoid molecules offer higher regulatory challenges. The manufacturing, safety, clinical and regulatory challenges of developing a novel cannabinoid botanical drug are compared to those of a new purified cannabinoid drug.

**11:50** *Complimentary Networking Lunch*

1:05 **Unlocking Cannabinoid Therapeutic Innovation by Advancing the Scientific Landscape**

***Terry O'Regan, President, Brains Bioceutical***

This presentation will summarize the course, challenges, considerations & rewards for scientific cannabinoid advancement.

## *Research Spotlight—The Promise of Novel Cannabinoid Drug Candidates*

1:45 **Novel Cannabinoid for the Potential Treatment of Traumatic Brain Injury and Neurodegenerative Disorders**

***Hunter Land, Vice President of Research & Development, Biopharmaceutical Research Company***

Abstract coming soon

2:25 **Development of a Synthetic CB2R Agonist as an Immunomodulator to Treat Hyperinflammation**

***Aurélia De Pauw, MSc, PhD, MBA, Tetra Bio-Pharma***

The CB2 receptor (CB2) expression is enriched in a wide range of immune cells, including those involved in the early innate immune response. CB2 activation is implicated in the induction of multiple anti-inflammatory pathways. We developed a drug candidate, ARDS003-PO, highly selective of CB2 for the treatment of hyperinflammation and prevention of acute respiratory distress syndrome. The drug substance, onternabez, demonstrated anti-inflammatory effects in rodent models of sepsis, SARS-CoV-2 infection, pulmonary fibrosis, vascular inflammation, and several other disease states where hyperinflammation drives progression or severity. Onternabez treatment decreased levels of pro-inflammatory cytokines (e.g. IL-6, TNF-□ and IL-1ß), chemokines (e.g. CXCL2, MIP-2 and RANTES), and other inflammatory mediators (e.g., ICAM-1 and VCAM-1), and also decreased indicators of inflammatory cell recruitment and organ damage or dysfunction. Additionally, onternabez exhibits mild anti-viral activity in vitro, a desirable property for the treatment of inflammation associated with viral infection. Thus, in multiple contexts, onternabez is positioned as a promising agent for the treatment of acute systemic hyperinflammation and prevention of inflammatory organ damage.

This presentation will highlight the early development stages of this new drug candidate, from preclinical evidence on its immunomodulatory, antiviral and antifibrotic properties to the development of an oral formulation suited for human administration and the regulatory trajectory and requirements for a first in human trial authorization.

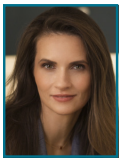
3:05 ***Afternoon Networking Break***

## *Panel Discussion*

3:45 **Identifying & Overcoming Challenges to Bringing Cannabinoid-derived Drugs to Market**

***Moderator: Michael Moussourakis, Alconox***




Panelists:
Aurélia De Pauw, Tetra Bio-Pharma
Hunter Land, BRC
Gosia Meunier, HAPA pharm
Karolina Urban, Avicanna

Participants: The Audience

4:20 **Best Practices for Ensuring Patient & Consumer Safety in Cannabis and Cannabinoid-derived Pharmaceutical Products—A Novel Approach for Cleaning and Disinfection**

***Dijana Hadziselimovic, Technical Services Laboratory Specialist, Life Sciences Division, STERIS***

This discussion provides an overview in building quality into cannabis production and manufacture of cannabinoid-derived pharmaceutical products to reproducibly deliver therapeutic benefit and the role of cleaning validation plays in product consistency and use of best practices adapted from pharma to control your tissue culture, cultivation, and cGMP manufacturing process environments resulting in fewer lost batches and reduced costs. The attendee will have a greater appreciation of contamination control with respect to the environment and equipment by understanding what "clean" means so you can better defend your process to inspectors, auditors, and investors, cover time-kill data for common disinfectants, discuss pesticide removal. Best practices and a novel approach for equipment cleaning to optimize cleaning processes to ensure your extraction equipment is efficiently cleaned to produce quality product that is safe for consumers and more importantly, patients, will be covered in detail leading to improved contamination control in cannabis cultivation and extraction processes and meeting regulatory requirements at each of these stages.

4:55 ***Happy Hour Mixer***

Join us in the lounge for informal networking. Complimentary appetizers provided.

## Wednesday, June 21

**7:30** *Complimentary Breakfast*

Conference Keynote

**8:30** ### Where the Grass is Greenest: Using Observational Data to Inform Cannabinoid-Based Clinical Trials

***Dr. Staci Gruber, Director of Cognitive and Clinical Neuroimaging, McLean Hospital, and Associate Professor of Psychiatry, Harvard Medical School***

Despite increasing popularity and access, in the United States cannabis has had a rather storied past, from its inclusion within the US pharmacopeia in 1850 to its classification in the most restrictive class of the Controlled Substances Act in 1970, where it remains to this day. Accordingly, for decades, data regarding the impact of cannabis have largely been derived from observational studies of recreational consumers or acute administration studies using products sourced from the National Institute on Drug Abuse (NIDA), and studies of medical cannabis, while expanding, have historically been limited. Given the paucity of data regarding the long-term impact of cannabis for medical purposes, Dr. Gruber founded the Marijuana Investigations for Neuroscientific Discovery (MIND) program, designed to examine the long-term impact of medical cannabis use on a range of health-related outcomes using a number of different methodological designs, including observational, longitudinal studies as well as clinical trials. While clinical trials are often considered "the gold standard," the importance of high-quality observational studies cannot be overlooked, as data from these studies inform the formulation of products that are optimized for specific conditions or indications. During this presentation, Dr. Gruber will share findings from the MIND program's flagship observational, longitudinal study and discuss how these data have informed the MIND program's Investigational New Drug (IND) applications and subsequent clinical trials using novel, custom formulations.

## *Research Spotlight—Oral & Topical Formulations*

**9:15** ### Lipid-based Formulations for Oral and Topical Delivery of Cannabinoids

***Inayet Ellis, PhD, Scientific Affairs Director, Gattefossé USA***

Lipid vehicles are natural way in development of cannabinoid formulations to improve bio-efficiency. While improving bio-efficiency, the formulators must also give attention to their stability and manufacturing aspects of the cannabinoid formulations. In this talk, formulation screening procedures for THC and CBD will be covered to optimize oxidative stability and bioavailability of cannabinoids for efficient oral and topical delivery. Case studies will demonstrate enhanced topical penetration/permeation and oral bioavailability with SEDDS formulations.

**9:55** *Morning Networking Break*

**10:25** ### Topical Delivery Formats of Cannabinoids for Dermatological Conditions and Musculoskeletal Pain and Inflammation

***Karolina Urban, Vice President of Scientific and Medical Affairs, Avicanna***

Abstract coming soon

**11:05** ### Critical Considerations for Emulsified Cannabinoid Formulations

***Matthew Elmes, PhD, Director, Green Analytics***

Emulsification of cannabinoid APIs has become an increasingly prevalent formulation strategy in recent years due to various benefits including permitting long-term aqueous solubility and displaying attractive pharmacokinetic properties. Oral consumption of emulsified cannabinoids significantly improves their bioavailability, quicken onset time, and allows the API to partially bypass hepatic first-pass effects by promoting lymphatic uptake. Cannabinoid emulsion formulations are highly suitable for many diverse form factors and are particularly useful for the creation of fast-acting edibles, infused beverages, and spray-dried powders.

However, formulators utilizing emulsified cannabinoids must give extra scrutiny to their formulation strategies as cannabinoid emulsions are subject to various physical and chemical degradation processes not seen in typical cannabis oil formulations. Hydrophobic cannabinoids residing in emulsion particles forces their exposure to the aqueous phase at the oil-water interface, causing significantly higher rates of oxidative chemical damage to the API. Furthermore, cannabis-infused beverages are subject to physical loss via adsorption of the cannabinoids to most common can liner materials. Often infused beverage products, even in legal markets with a valid COA, exhibit drastically reduced potencies by the time it reaches the consumer. Many medical cannabis patients today rely on accurately labeled products from their local dispensary, but the widespread inconsistent potencies of infused beverages can be problematic for their treatment regimens.

The work presented here provides an in-depth overview of modern formulations strategies and other considerations to protect the chemical and physical

stability of cannabinoid emulsions. Our patent pending strategies allow for >1 year room temperature shelf life of cannabis beverages with no detectable potency loss. Gold-standard quality control procedures recommended for manufacturers to ensure high-quality emulsion products, such as monitoring particle size, zeta-potential and liner compatibility, will also be reviewed.

11:45 *Complimentary Lunch*

1:00 **Critical Cleaning: The Key to Quality & Safety in Cannabinoid-derived Pharmaceutical Applications**

***Michael Moussourakis, Senior Director, Strategic Affairs, Alconox***

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, resinous, 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.

## *Research Spotlight—Therapeutic Ensembles*

1:35 **Cannflavins Mechanism of Action on Inflammatory Pathway/Cannflavins Dual Inhibition of the Pro-inflammatory Pathway**

***Akeem Gardner, Founder & CEO, Canurta, Inc. [Co-authors: Eric Soubeyrand, Kelly Boddington, Cameron Parry, & Jose Casaretto, Canurta, Inc.]***

Hemp derived flavonoid, namely cannflavins have been linked to the cannabis therapeutic properties but are present in extremely low concentration in planta. At Canurta we developed the analytical capabilities to screen cannabis sativa germplasms for cannflavins and to enrich them, taking advantage of proprietary technology to extract these polyphenols from the plant. Here, we decipher the mechanism of action of cannflavins on the inhibition of pro-inflammatory pathways. On a molecular level, the Inflammatory stimuli activate the two main branches that lead to inflammation: leukotrienes (5-LO) and prostaglandins (PGES). Cell-free in-vitro enzymatic assay using mPGES-1 (prostaglandin E2 synthase-1) enzyme from human cell line A549 derived microsomes demonstrates that cannflavins directly inhibit the prostaglandins pathway (mPGES-1). Uniquely, cannflavins inhibit the other inflammatory branch pathway (leukotrienes) in a 5-LO cell-free assay using human monocytes and performed similarly to the commercial drug Zileuton, a leukotriene inhibitor. In-follow, cell-based assays are currently performed to confirm the cell-free work. To translate the in-vitro assays we studied various in-vivo models of inflammation, where the properties of cannflavins for pain management and to measure their ability to combat the immune response from infection.z

2:15 **The Cannabis Entourage Effect: A Dive for Scientific Truth**

***Marilyn Barrett, PhD, Founder & Principal, Pharmacognosy Consulting***

The definition of an entourage is a group of attendants or associates that surround a person of rank or importance. For cannabis, the term has come to represent a theory wherein the chemical constituents in cannabis combine to produce a greater effect than when delivered separately. Dr. Mechoulam's team in 1998 coined the term "entourage effect" when they discovered that two endogenous 2-acyl-glycerol esters, which did not bind to cannabinoid receptors on their own, were able to potentiate the binding of an endocannabinoid (2-arachidonoylglycerol) to both CB1 and CB2 receptors. In 2011, the cannabis entourage concept was popularized by Dr. Ethan Russo when he explored the combination of cannabinoids with terpenes in the plant. Since then, the concept has grown to apply to the potential for cannabinoids, terpenoids and flavonoids to work in concert to create an effect beyond that of the pure compounds. But what do we actually know scientifically? The evidence, like the chemicals themselves, is complex. There are possibilities for pharmacodynamic interactions on one or multiple cellular targets (additive, synergistic or antagonistic). There are possible pharmacokinetic effects on bioavailability, metabolism and distribution. Also, the potential for alteration of side effects from one compound by another. Is it time for us to use science to dive into this concept to see what applies and what does not? The debate on the therapeutic use of pure isolated compounds vs chemically complex preparations from plants has raged since the disappearance of plant medicine from mainstream American medicine in the early twentieth century. Let's pose questions that provide a road map towards the scientific truth.

2:55 *Afternoon Networking Break*

## *Technology Spotlight—The Role of CBD-loaded Exosomes in Potential Cancer Treatment*

3:10 **Role of Cannabidiol-loaded Exosomes in TNBC and Chemotherapy-induced Peripheral Neuropathy**

***Mandip Sachdeva, Professor and Section leader, Pharmaceutics, College of Pharmacy, Florida A & M University***

Cannabinoids (Δ9-THC and CBD) are gaining enormous interest in cancer due to their potential effects on regulating cancer cell proliferation, metastasis, angiogenesis, and differentiation. Accumulating evidence demonstrates the therapeutic efficacy of CBD in preclinical and clinical models of breast, gliomas, lung and other cancers. Apart from CBD, other minor cannabinoids like THCV, CBG are also being investigated for their role against chemotherapy resistant cancers. Exosomes or small EVs (vesicles of 30–150 nm) are produced by the invagination of endosomal membranes (i.e., multivesicular bodies) and their subsequent fusion with plasma membrane. Larger EVs are shed from the cell surface and called microvesicles. Recently, EVs have gained much attention for their potential use as drug delivery system (DDS) in various diseases. Apart from their extraordinary roles in mediating cell–cell communication, EVs (endogenous nanovesicles) are promising drug carriers for both hydrophilic (such as siRNAs and miRNAs) and hydrophobic drugs in cancer because of their high stability and biocompatibility. EVs derived from hUCMSCs (hUCMSCs-EVs) are gaining tremendous attention due to their potential clinical applications in various conditions such as cancer, bronchopulmonary dysplasia, pulmonary hypertension, organ/tissue injury, stroke, liver fibrosis, wound healing, Alzheimer's disease, chronic kidney repair, liver fibrosis, acute inflammation and blood glucose level regulation by shuttling various bioactive components (proteins, lipids, mRNA, miRNA, and DNA) during mediation of cell–cell communication. However, EVs production through bioreactors with hMSC culture has not been widely reported as a potential feasible strategy.

As both CBD and hUCMSCs-EVs are well demonstrated in amelioration of cancer, this presentation will demonstrate the role of therapeutic usage of hUCMSCs-EVs generated from PBS-VW bioreactors as an ideal delivery platform not only for improving the absorption and bioavailability for CBD but also for the reduction of CBD dosage required to achieve tumor regression especially in resistant TNBC cancers.

Further their role in overcoming chemotherapy induced neuropathy will also be discussed.

3:50 **Antares Presentation**

***Heath Miller, Product Manager, Antares Health Products***

Abstract coming soon

4:30 *Close of Program*

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