

**USP-ASTM Global Workshop on Cannabis Quality
Part I – America and Europe
December 7–8, 2022**

The notes of this meeting are provided as an informal resource. They are not meant to provide a transcript of the proceedings, do not reflect any determinations or policy on the part of USP, ASTM or other participants, and should not be used as an interpretation of USP compendial standards.

DAY 1 (8:00 a.m. to 12:15 p.m.)

Dr. Nandakumara Sarma, PharmD., USP

Dr. Sarma welcomed attendees and emphasized the following:

- Introduced USP
- Provided an overview of the objectives of the meeting with focus on medical use of cannabis:
 - Obtain awareness of the existing data and regulatory framework for cannabis quality and public quality standards on defining cannabis product quality attributes globally – initially from a North American and European perspective
 - Understand the scientific basis for standards to explore potential harmonization amongst the standards groups
 - Facilitate discussions between stakeholders to identify needs and challenges related to cannabis quality
 - Identify areas of global data gaps to inform future standards and research needs
 - Identify the topics that deserve a deep dive conversation and address those topics in future events
 - Disseminate proceedings of this workshop

Mr. David Vaillancourt, M.Sc., ASTM International

Mr. Vaillancourt emphasized the following:

- USP has been a committed and key organization at the table since ASTM International first put out a call for interested stakeholders to meet in West Conshohocken, PA, in late 2016 to discuss the feasibility and need to form committee on cannabis. This workshop builds on that day and the historic milestones since then.
- The importance of public health and safety is a key driver of what has brought workshop participants together.
- Producers, users, regulators, and researchers have a vested interest in ensuring that all medicines and decisions around them are rooted in evidence and best practices.
- The continued call for standardization of cannabis in the United States and internationally has accelerated since 2016. The history of cannabis as a medicine predates all of this by millennia.

Regulatory Panel

Chair: Julio Sánchez y Tépoz, M.Sc., JD, former Head Commissioner of COFEPRIS (Mexican Ministry of Health)

The Chair introduced the panelists: Werner Knoess, Ph.D., German Federal Institute for Drugs and Medical Devices (BfArM); Joao Perfeito, M.Sc., Brazilian Health Regulatory Agency (ANVISA); Andrew Wayne, Ph.D., Health Canada

Chair emphasized the following:

- For many years in Mexico, cannabis was considered a plant that was prohibited for everyone. It took some time for regulators and legislators to understand that there was very strong support for considering cannabis for its therapeutic effect.
- We should be working more on clinical trials and considering standards. For FDA and other global regulators, there should be robust documentation and research to help assure quality, efficacy, and security of the medical supplies of cannabis.
- For regulators, there should be sufficient scientific consideration to give and issue market authorization. This has been the greatest challenge for regulators.
- In Mexico there is very strong regulation of medical cannabis, but there has not been any application to authorize these products. Market authorization requires applicants to present clinical studies to demonstrate quality, efficacy, and security of the products.
- The gaps in knowledge and differences in the regulatory framework make harmonization between nations challenging and present obstacles to consumer access to products in the marketplace.

Andrew Waye, Ph.D., Health Canada

Dr. Waye emphasized the following:

- Overview of quality requirements of cannabis products in Canada.
- Two paths to bring cannabis to market in Canada:
 - Cannabis products that are subject to the Cannabis Act and its regulations
 - Drugs containing cannabis for human or veterinary use
- Provided an overview of the Cannabis Act including cannabis regulations, health, and safety measures
 - Four main classes of cannabis products: dried cannabis, cannabis extracts including inhaled forms, cannabis topicals, and edible cannabis
 - General quality control requirement for all products:
 - Accurate testing and labeling of THC and CBD in finished product testing.
 - Chemical and microbial contaminants specified within established limits taking into account how the product is consumed.
 - If using accessories, they must not contaminate the cannabis.
 - Testing must occur at or after the last step when contamination is likely to be introduced or concentrated.
 - Testing for pesticide active ingredients is mandatory for cannabis.
 - Cannabis contamination testing includes tests for mycotoxins, elemental impurities, microbial contaminants, foreign matter, residual solvents, and pesticides.
 - Timing of testing occurs at or after the last step in which contamination could occur; for edible cannabis, testing must be on input cannabis.

- Mandatory cannabis testing for pesticide active ingredients (list of 96 pesticides) to ensure no unauthorized use of pest-control products. Timing of testing has to occur on harvested cannabis (fresh or dried).
- Requirements for contaminants are general. They are designed in a way that is applicable to any and all chemical or microbial contaminants, on a case-by-case basis.
 - It is necessary to understand the production processes and inherent risks of contamination for each product.
 - Health Canada has issued ad hoc guidance where requirements may be unclear to license holders.
- Leverage or align with existing frameworks where appropriate.
 - Edibles align with food requirements; topicals align with cosmetic requirements.
 - Leverage or apply existing standards (e.g., pharmacopoeias) on a case-by-case basis.
 - Align with existing Health Canada frameworks for evaluating risk.

Joao Perfeito, MSc, Brazilian Health Regulatory Agency (ANVISA), Brazil

Mr. Perfeito emphasized the following about the Brazilian experience regulating cannabis:

- Brazil is a signatory of the U.N. conventions (as are all of the nations represented in this workshop).
- Cannabis for smoking, food, and cosmetic is not allowed in Brazil; Cannabis is allowed only for medical use and scientific purposes; however, there is no law in Brazil dealing with the cultivation of cannabis for medical purposes.
- Brazil does not have a regulatory framework regarding the cultivation; therefore, it is not a possibility in Brazil.
- In accordance with Resolutions RDC 26/2014 and 24/2011, as herbal medicines or as isolated or purified herbal substance, the possibility of import cannabis-based products licensed in other countries was established. Initially, considering the growing demand for cannabis for treatments, Resolution RDC 17/2015 was published establishing a procedure for importing products licensed in other countries by an individual, for their own use, upon prescription by a legally qualified healthcare professional.
- Increasing demand for cannabis-based products is notable with demand quadrupling in the past 6 years. There are no quality requirements applied to imports for cannabis-based products for patients.
- In a strategy to improve access to cannabis-based products; a channel for clarifying doubts from consumers and prescribers; to establish monitoring and pharmacovigilance; commercialization of products with adequate quality for use; and availability of adequate product information to patients and prescribers, ANVISA published a new Resolution (RDC 327/2019) resulting from a discussion based on benefit - risk relationship, providing for the authorization of products that follow all technical requirements applied to medicines, except for the complete safety and efficacy dossier.
- Provided an overview of Resolution RDC 327/ 2019, which established the definition of cannabis-based products for medical use as a new class of product that does not follow the regulatory pathway for medicine.
 - It is mandatory to have labeling and packaging information on THC and CBD quantities.

- Provided an overview of requirements for authorization.
 - Technical and scientific rationale: formulation and route of administration.
 - Benefit-risk assessment plan.
- Provided an overview of quality control:
 - Cannabis-based products must follow all medical quality requirements.
 - Importantly, finished product QC must be carried out in the territory for all imported batches.
 - In case of monograph in official pharmacopeia, the monograph becomes mandatory.
 - *Brazilian Pharmacopoeia* is discussing a proposal for a monograph on *Cannabis sativa L.* inflorescence.
- Provided an overview of herbal medicines quality control (QC) for raw materials, excipients and packaging materials and finished products.
- Isolated substances of herbal origin QC.
- Stability tests include those for the drug substance and product, storage conditions, intermediate conditions, long-term stability, and photo stability testing.
- Provided an overview of Analytical monitoring programs that systematically monitor analytical QC data of cannabis-based products sent to ANVISA by the responsible analytical laboratories and carry out guidance and fiscal analyzes on samples of cannabis-based products and medicines containing CBD and THC.
- Future perspectives:
 - Improvements as a continuous process
 - Review of Resolution RDC 327/2019 in course.

Chair: I have seen the publications in social networks and it is impressive that you are considering monograph information, and best practices around the world to give certainty to the Brazilian market to issue authorization for cannabis products. The Brazilian regulatory agency has been doing very good studies and work.

Werner Knoess, Ph.D., Head of German Cannabis Agency BfArM (Federal Institute for Drugs and Medical Devices)

Dr. Knoess provided a presentation on medicinal cannabis in Germany that emphasized the following:

- Provided background on the establishment of the Cannabis Agency to control cultivation and supply of medical cannabis in Germany.
- Among the key elements of the new legal framework in 2017, patients with severe illness should have improved access to products prescribed by doctors with reimbursement and pharmaceutical quality.
- Provided an overview of Division Licensing 4 at BfArM.
- Subsection 55 of the German Medicines Act and the *European Pharmacopoeia (Ph.Eur.)* are both relevant for the development of medical cannabis.
 - *German Pharmacopoeia* published on monograph cannabis flowers DAB.
 - In the *Ph.Eur.* there is ongoing discussion about a monograph defining quality of cannabis flowers.

- BfArM – Cannabis Agency for the control of medicinal cannabis in Germany and adequate distribution (e.g., including steps for technology and security from growth, pre-cultivation, harvest, processing, testing, storage, packaging, supply, distribution across Germany to pharmacies and patients).
- Noted the typical contents of monographs for Quality cannabis flowers (e.g., characteristics, purity, assays, odor, foreign matter, loss on drying, identification, cannabinoids, pesticides).
- Noted that Background documents are available for herbal medicinal products (e.g., legal definitions, guidelines on quality and specifications, irradiation).
- There is a dynamic in the cannabis market that demands flexibility on how to deal and develop the system.

Chair: There are gaps in regulations, but it is important for regulators to be sure that quality and efficacy are well demonstrated. That applies not only to cannabis products but also for medicinal products all over the world so the same conditions applied to demonstrate efficacy, quality, and security around the world should be demonstrated as well for cannabis products for medical purposes. In that context, there are several regulatory gaps. Work has been going on for decades to harmonize regulations because it is a best practice and also because harmonization would reduce obstacles. Regulators understand that harmonization is good but is very difficult. Let's think about convergence to the same objectives and think about reliance. For example, in Brazil, ANVISA relies on pharmaceutical concepts established in several major pharmacopeias.

Regulatory Panel Questions and Discussion

Q: What are some of the gaps and differences in frameworks that make harmonization between nations/member states challenging?

A: Werner Knoess: We may have scientific discussion as a first step to convergence. Everyone wants to assure the quality, safety, and if relevant, the efficacy of medical products so this is a starting point for convergence. First steps toward reliance would not be a scientific problem but would require whether regulators could rely on others with a range of similar but different regulatory systems. We can discuss convergence on a scientific level; reliance on regulations will take some time because of different legislations' views.

A: Andrew Waye: For a cannabis drug, we are closely harmonized and recognize/acknowledge EU, U.S., and Canadian good manufacturing practices (GMPs). For a drug/therapeutic cannabis product, there is already convergence as for any other drug. The differences really are for cannabis for recreational purposes. When you put a health claim on the product it is a drug subject to a widely adopted standards. For therapeutic products with a health claim, we are probably already on the right path.

Chair: What you said about convergence on a scientific basis is important. That's a key challenge for industry. We need clarity related to the classification of the products.

Q: How is ANVISA dealing with this classification and how is it dealing with the analysis of the technical requirements in our cannabis processes for authorization?

A: Joao Perfeito: This is a challenge in Brazil; there are no regulations for cultivation because cannabis is restricted to medical and scientific purposes. Many member states have different regulations and it is very difficult to harmonize regulations. The way the country views regulations that are applied to medicines (e.g., technical requirements, GMPs) make regulatory work more complex and challenging. The biggest challenge of the cannabis-based product is to achieve a balance between guaranteeing that patients have access to products that they need and controlling the risks related to the use of those products. We have been trying to converge with regulations for herbal medicines.

Chair: In Mexico in 1938, there was a decree by which the ministry of health prohibited substances that affect the soul of the users. Now many years after that, the Mexico Supreme Court established that the provision of cannabis for individual purposes is not a necessary measure for public health. There are great opportunities for regulatory convergence as well as reliance on international standards, including the USP monograph.

Q: What are your thoughts about standardization of technical requirements for medical cannabis?

A: Andrew Wayne: In Canada, our regulations are high level and do not specify test methods and contaminants. Regulators don't always incorporate a specific standard as a requirement. Our standards are tools in a toolkit for industry and regulators. The standards are there to help people demonstrate compliance. Increased standardization helps regulators assess and identify risks and helps industry meet validation requirements for cannabis. If a standard misses a contaminant the license holder is not off the hook for that contaminant.

A: Werner Knoess: In Europe, we are stricter about what regulations are necessary. Different standards can be a matter of scientific debate, and there are mechanisms to develop monographs in the *German* and *European Pharmacopoeias*. In Germany, we have individual precision, but we do not see proof of efficacy of cannabis flower. This might be judged differently in Europe. This is why the field of cannabis is diverse. The quality issue is mostly a good starting point to agree on quality issues and go a step further. There are ongoing discussions on cannabis in the U.N., which also has to be taken into account. From a scientific point of view, the more we have convergence of standards, the better we have preconditions for global exchange.

A: Joao Perfeito: The establishment of monographs for herbal products could provide clarity for material and finished products, and we are looking at those at this moment. Scientific data are now being produced that will help us determine some specifications and limits for contaminants based on exposure to products. It is important to pay attention to those results and work toward improvement of those parameters and the harmonization process.

Chair: Maybe the challenge is how to rely on different contexts for regulators and patients.

Q: What is your experiences on this in Netherlands?

A: Marco van de Velde, Ph.D., Dutch Office for Medical Cannabis, the Netherlands : It is important to have products free of contamination. We have at this moment dried flowers available and some cannabis oil; no extracts. It must be free of pesticide and other contamination.

Chair: In many countries, the cannabis movement started because there was a movement from parents of children with health problems. That's why in Mexico in 2015, claims were presented to the ministry of health to give opportunities for import of products with cannabis from the U.S.

Q: What is the balance between direct patient access to those products and safety, security, and efficacy of cannabis? We as regulators think about science and technical requirements, but there are patients who need these products. What is your opinion about balancing technical requirements and patient access?

A: Andrew Wayne: Cannabis has been accessible to patients for 20 years through healthcare providers. It is readily available to people who need access to cannabis as well as medicines that undergo the drug pathway for health claims. Our framework tries to strike a balance between having cannabis accessible to those above a certain age who need it with or without a healthcare provider. We have a balance because there was strong cannabis use in Canada. We also allow import into Canada for scientific and medical purposes with consultation with a healthcare provider. Access regulations followed court decisions.

Chair: You demonstrated very good regulations and scientific support for decisions. In Canada there is a very good reference for regulatory challenges in the cannabis area.

Q: What do you think about the balance between patients' needs and the regulations?

A: Joao Perfeito: We do not have complete regulatory data on medical cannabis-based products. We need information on safety, efficacy, legal, and regulatory considerations as we do not have complete data for the wide diversity of these products or the situations where they are used. It is necessary to have resolution of use for cases without therapeutic alternatives. It is very complex. We are facing a challenging moment trying to consider how to access balance with the scientific information about those products.

A: Marco van de Valde: We have five varieties available in prescription. There is a need to be counseled by the pharmacist and prescriber.

Chair: There is an opportunity to prescribe and to access the products.

Q: What are your thoughts about these balances regarding the medical doctor that prescribes cannabis products and is there a need to educate more doctors to prescribe medical drugs containing cannabis?

A: Werner Knoess: We are seeing the development of education for medical doctors and pharmacists in the use of cannabis products for patients. Under current legislation and from monitoring pharmacovigilance, we have some insight about quality and safety and that access is working. There is a need for further scientific, quality, and efficacy data to help inform future discussions about their classification and status as medicinal products. Most important, when you focus on patients, there are options and the possibility to provide them with products and ongoing network supporting development. We need more and better clinical data.

Chair: There are some important challenges to regulate and authorize medical cannabis products. We are on a road where regulators should be more open to converge, harmonize, and rely on the regulatory systems. I believe that reliance is an opportunity for all regulators to see opportunities created by advanced regulatory systems. We as regulators work for patients. Our principal goal is to deliver products with efficacy and security that are based on technical and scientific grounds. And we have a challenge in terms of relying on our regulatory systems.

Dr. Sarma summarized the Q&A session, emphasizing that panelists talked about harmonization, convergence, and reliance along with similar objectives based on science. Dr. Sarma introduced the concept of scientific alignment based on science and best practices. This requires much larger discussion and needs to be a topic for follow-on, deep dive discussions.

STANDARDS PANEL

Chair: Robin J. Marles, Ph.D., Health Canada

The Chair emphasized the following:

- Public standards can set specifications for identity, cannabinoid content, limits for contaminants, and other quality attributes.
 - Standards are fundamental to meeting the challenges of test methods that are not validated, inaccurate label claims for cannabinoid content, varying limits for microbial and chemical contamination, and emerging concerns related to synthetic minor cannabinoids and impurities.
- Documentary standards (i.e., pharmacopeial or compendial standards) articulate agreed-upon testing methods and acceptance criteria used in quality assurance and quality control protocols.

- They provide benchmarks to evaluate an article's identity, purity, strength, and performance. They provide transparency on quality expectations for the article. They can be utilized by any stakeholder to help assess the quality of their products.
- Reference standards are physical samples consisting of a known quantity of a substance or ingredient, developed in alignment with the specifications outlined in the corresponding documentary standard.
 - They undergo rigorous testing in a collaborative study and are subject to statistical analysis. These standards come in small vials and enable manufacturers to test their product against the standards to ensure it meets published specifications.
- The Chair highlighted examples of recent work on cannabis standards from ASTM Committee D37; USP Botanical Dietary Supplements and Herbal Medicine Expert Committee and its Cannabis Expert Panel; the Netherlands Office of Medicinal Cannabis; the German (2017), Danish (2019), and Swiss (2019) Pharmacopoeias; EDQM; and American Herbal Pharmacopoeia.
- Diverse and complementary standards are needed, but clear lines of communication must be maintained to prevent duplication or wasting of precious resources.
- The Standards Panel for the ASTM–USP Global Workshop on Cannabis Quality is a step in the right direction as a forum for conversations toward promoting regulatory convergence or harmonization to the extent possible given our different legislative and regulatory frameworks and areas of expertise.

The following panelists presented information on standards resources (e.g., monographs, reference standards, guidelines) and the current priorities for cannabis quality from their organizations.

Nandu Sarma, Ph.D., USP

Dr. Sarma emphasized and provided information on the following:

- Articulating quality attributes for cannabis inflorescence helps prevent harm to patients.
- Provided a timeline of cannabis-related activities over six years of stakeholder events.
- USP has commented on cannabis quality to federal regulators and others.
- Presented an overview on USP compendial activities and proposed cannabis standards
- Described critical components of botanical quality, including critical quality attributes.
- Noted CBD quality attributes as indicated in *PF* proposal for CBD API monograph in *PF* 48(1).
- Noted that *USP* General Chapter <1568> *Quality Considerations for Cannabis and Cannabis-Derived Products for Clinical Research* prospectus was posted on USP.org on May 27, 2022.
- Noted Quality attributes for cannabis inflorescence in the *Journal of Natural Products*.
- Noted that the *USP Herbal Medicines Compendium's* proposed Cannabis monograph is open for public comment.
- Provided an overview of USP's work on Cannabinoid profile for identification, criteria for chemotype classification, tests for identification and cannabinoid content, and quantitation of the cannabinoids.

David Vaillencourt, MSc, Vice Chair, ASTM Committee D37 on Cannabis

Mr. Vaillencourt emphasized the following ASTM international and cannabis industry standard developments:

- Introduced ASTM international in its role facilitating the development of voluntary standards and the work of Committee D37.
- Committee D37 on Cannabis was formed in 2017, has more than 1,200 members in more than 30 countries, 10 technical subcommittees, and 48 approved standards. Notable standards include:
 - D8197-22: Standard Specification for Maintaining Acceptable Water Activity (aw) Range (0.55 to 0.65) for Dry Cannabis Flower Intended for Human/Animal Use
 - ASTM D8309-21: Standard Guide for Stability Testing of Cannabis-Based Products
 - ASTM D8439-22: Standards Specifications for Medicinal-Use Cannabis Inflorescence
 - D8450-22: Standard specification for environmental conditions while packaging cannabis/hemp flower
 - D8334-20: Standard practice for sampling of cannabis/hemp post-harvest batches for laboratory analyses
 - D8452-22: Standard guide for requirements for medical-related professionals within the cannabis and hemp industries.
 - D8469-22: Standard test method for analysis of multiple elements in cannabis matrices by inductively coupled plasma mass spectrometry (ICP-MS)
 - And much more in development including test methods and sampling and process methods
- Noted work going forward to establish an international symbol for all consumer products containing intoxicating cannabinoids (now published as D8441-22).

M.J. van de (Marco) Velde, Ph.D., Dutch Office for Medical Cannabis, the Netherlands

Dr. Van de Velde provided a presentation on quality issues and medicinal cannabis in the Netherlands and emphasized the following:

- Overview of work on cannabis began in 2003 with pressure from society (patients, patient groups, parliament) against the prohibition of medicinal use.
- The ministry of health installed a national office, the Office of Medicinal Cannabis (OMC), with the following key responsibilities:
 - Ensure that the quality of medicinal cannabis produced meets pharmaceutical standards.
 - Establish an effective procedure for distribution compatible with rules for Good Distribution Practices for registered pharmaceutical products.
- Provided an overview of indoor vs outdoor cultivation
- Noted current priorities for cannabis quality
 - Adhere to coming *Ph.Eur.* monograph on cannabis flos (i.e., set for metals)
 - Optimization of harmonization of cannabis flos
 - Discussion of harmonization-standardization of good processes for cannabis flos
- Medicinal cannabis complies with pharmaceutical quality guidelines
 - Standardized product with constant content
 - Very low concentration of degradation compounds (e.g., CBN)
 - Free of contamination with micro-organisms, pesticides, heavy metals and aflatoxins

Jaume Sanz-Biset, Ph.D., European Pharmacopoeia (Ph. Eur.), EDQM, France

Dr. Sanz-Biset provided a presentation on the European Pharmacopoeia as a whole, that afterwards focused on the draft monograph on Cannabis flos published in *Pharmeuropa* 34.4. With regards to the latter, the presentation emphasized the following:

- Welcoming pertinent users to submit comments on the text published in Pharmeuropa (deadline 31 December 2022).
- The definition section being based on the description of ad-hoc specifications for content for 3 different types/chemotypes of *Cannabis sativa* L.
- Statement in the Production section on minimizing the presence of stalk in the herbal drug only applicable when the herbal drug was prescribed to patients (thus excluding herbal drug used for extraction, i.e. used for the preparation of extracts).
- On identification by HPTLC, the requirement to obtain in the chromatogram more intense bands for Δ^9 -THCA than Δ^9 -THC, and for CBDA than CBD.
- On the proposed HPTLC-UV procedure, the prescription of two reference substances, i.e. *cannabidiol for cannabis CRS* (for quantitative use only) and *cannabis flower for system suitability HRS* (for qualitative use only).
- With regards to the test for total CBN, the prescription of three different system suitability test acceptance criteria, based on the separation of three different chromatographic pairs due to CBG and CBDA, CBGA and Δ^9 -THC, as well CBNA and CBC.
- Additional requirement for the test for foreign matter only applicable when the herbal drug was prescribed to patients, based on excluding the presence of seeds and leaves more than 1.0 cm in length.
- With regards to the assay, the prescription of one system suitability test acceptance criteria, based on the separation between CBD and CBDA.
- Noted that a Ph. Eur. monograph was not a stand-alone text and must be read in conjunction with the *General Notices*, pertinent general texts and applicable general monographs. Of particular importance for the draft monograph on cannabis flos were 1433 *Herbal drugs*, 20813 *Pesticide residues*, 20802 *Foreign matter*, 50108 *Microbiological quality of herbal medicinal products for oral use and extracts used in their preparation*, and 50104 *Microbiological quality of non-sterile pharmaceutical preparations and substances for pharmaceutical use*.

Standards Panel Questions and Discussion

Q: Do you know when a final monograph might appear in the Ph Eur?

A: Jaume Sanz-Biset: This cannot be known yet. The next step will be for the Ph Eur expert group to address the comments that would be received during Pharmeuropa enquiry. This will take place in the meeting of this group planned for April 2023. In case the draft monograph does not need to be significantly modified after Pharmeuropa enquiry, the soonest the draft monograph would be able to be submitted for adoption by the Ph Eur Commission will be June 2023, thus implying that the earliest possible publication of the text in the Ph Eur would be in Supplement 11.5 (i.e. publication date: January 2024; implementation date: 1st July 2024).

Q: Standards that are in development for cannabinoids and the entourage effect, and asked if anyone would like to comment on standards that are developing for terpenoids, minor cannabinoids, and the entourage effect?

A: Nandu Sarma: This was discussed in our publication regarding the gap in research on minor cannabinoids. Appropriate qualification of the investigational material is important, so *USP* General Chapter <1568> could help in that regard.

A: David Vaillencourt: One of the things with standards, especially ASTM's D8439, is the requirement for labeling cannabinoids present above 10 mg/gram (consistent with *USP* recommendations) while recognizing that you have to characterize the 100% makeup of the product and quantify and evaluate the safety and consistency of the product.

Q: That is helpful. There was a question about labeling with cultivars. The challenge is that while there are well established industrial hemp cultivars, many of the medicinal cannabis strains are not as well characterized or formally classified as cultivars. The tremendous variability of cannabinoids and other components do not line up well with strains and colors (e.g., purple kush) so that is a challenge. Water activity vs drying to a specific level determined through loss of water is important. Could you address these terms?

A: Nandu Sarma: Our publication described those concepts well and that cannabis should be evaluated based on validated methods. Given the unique nature of the cannabis, cannabinoids are subject to decarboxylation. Water is controlled in such a way that it is not too dry, not too watery, which was described in detail in our publication.

Q: What are the specifications for total aerobic count and total fungi compared to setting specs for foodborne pathogen species.

A: Nandu Sarma: Total aerobic count is a surrogate for how the material is processed and harvested and collected. If there are more refined molecular methods for characterizing pathogenic microbes, USP staff would be happy to forward any information received on this topic to our relevant Expert Bodies for potential monograph updates as appropriate.

Q: We've received questions about GMPs and challenges of comparisons among jurisdictions. Are there government-certified GMPs?

A: Marco van de Velde: In the Netherlands, the health inspectors set it as an API producer. They ask for a GMP license and they do the audit and inspections according to the normal pharmaceutical GMP rules.

Q: There is a question about testing acidic forms of cannabinoids. Please comment?

A: Nandu Sarma: There are markers and chromatographic fingerprints supported by Reference Standards for testing of the specific cannabinoids and their carboxylated forms. This topic is addressed appropriately in USP publications including with cannabinoids before and after decarboxylation using the Liquid Chromatography and Gas Chromatography-based methods. These methods help in testing acidic cannabinoids without conversion.

Closing Remarks

David Vaillancourt emphasized the following:

- We've covered a lot of ground and had more than 400 attendees and more than 150 questions, which we will work to summarize and address.

Day 2 (8 a.m. to 12:15 p.m.)

INDUSTRY PANEL

David Vaillancourt welcomed attendees and reviewed Day 1 presentations and themes as follows:

- We heard from senior regulatory officials in Brazil, Canada, and Germany
- Had standards panelists representing ASTM international, USP, the *Ph.Eur.*, and Dutch office of Medical Cannabis.

Nandu Sarma welcomed everyone and emphasized that participants' input is valuable for shaping the next steps. We heard that harmonization is desirable but a difficult path. What is needed is a conversation among all players and congruence of the same public health goals and reliance on science-based approaches. This could be the path forward that is acceptable to

all participants. We probably need to take up some low-hanging fruit where we can to make progress. We hope to receive valuable input today and to continue the conversation.

Chair: Holly Johnson, Ph.D., American Herbal Products Association Opening Remarks

The Chair noted that the panelists will present information on the industry experiences in meeting regulatory requirements and utilizing the available standards for medical cannabis quality. This will be followed by a panel discussion and Q&A on the current gaps and industry needs for standards and whether (and how) harmonization of standards will help industry and improve public health.

Alan Sutton, Jazz Pharma, UK,

Alan Sutton provided a presentation on control and characterization of botanically derived cannabis drugs. The presentation emphasized an overview of the Epidiolex CBD API manufacturing process and specification differences between semi-synthetic and botanical CBD. Mr. Sutton provided an overview of the final considerations for botanically derived cannabis drugs and emphasized the following:

- The three main elements for drug products are quality, safety, and efficacy. Clinical trials are expensive, and efficacy can be difficult to demonstrate. Patients often have an expectation of success based on anecdotal evidence. For any product aimed at people with a medical condition, quality and safety should be fundamental.
- Structural alerts have identified components above specific thresholds as defined in ICH Q3A that should be evaluated by structural alerts software. These include toxicology risk assessment and, for Sativex, screening for more than 100 compounds through structural alert software.
- Mr. Sutton provided an overview of what is needed to make claims about full or broad spectrum and the entourage effect about terpenes or flavonoids. This included information on concentration ranges, manufacturing processes, compound stability, interactions with excipients, and extractables and leachables in finished products.
- Recommendation to use the *USP*, *Ph.Eur.*, and ICH guidelines for impurities and conduct risk assessment of your process, and test appropriately based on those assessments.

Prof. Giovanni Appendino, Indena, Italy

Dr. Appendino provided a presentation on quality control of cannabis-derived prescription drugs. The presentation emphasized the following:

- Cannabis as a source of mainstream prescription drugs.
- Natural vs synthetic phytocannabinoids.
- The residual phytochemical complexity of cannabis extracts.

Prof. Appendino provided the following conclusions:

- For cannabis-based pharmaceutical products, origin as well as identity is important.
- The regulatory status of CBD needs harmonization between EU and U.S. in terms of origin (natural/semi-synthetic) and realms of use.
- Natural and synthetic phytocannabinoids can be distinguished based on residual chemical complexity (phytochemical vs synthetic) and isotopic contents.
- The qualification of an extract as a botanical drug substance requires interfacing GAP and GMP rules.

Tjalling Erkelens, Bedrocan, the Netherlands

Tjalling Erkelens provided a presentation on good medicinal cannabis cultivation practices. The presentation emphasized the following:

- Good Agricultural and Collection Practice (GACP) is the only set of requirements available to companies in the EU for the cultivation of medicinal cannabis.
- Because GACP is insufficient for cannabis intended for medical use, Bedrocan developed a new practice for medicinal cannabis cultivation called Good Medicinal Cannabis Cultivation Practice (GMCCP) for the cultivation of medicinal cannabis.
- The purpose of the GMCCP standard is to increase the quality of medicinal cannabis cultivation and to get it as close as possible to GMP, while simultaneously taking into consideration the complexity of cultivating the cannabis plant for medicinal and scientific use.

Marcel Bonn-Miller, Ph.D., Canopy, Canada

Dr. Bonn-Miller provided a presentation on the industry perspective on cannabis quality and regulation. Dr. Bonn-Miller emphasized the following:

- The distinction between medicinal and recreational cannabis is false; most people use cannabis for both reasons and therefore tight standards for medical cannabis need to also apply to recreational cannabis.
 - Public health risks including dose-label inaccuracy.
 - Intentional and unintentional (e.g., leaching heavy metals or other contaminants from rubber gaskets inside cartridges) contamination issues. Testing of final products is needed.
 - Product packaging concerns need attention to mitigate unintentional ingestion.
 - Industry claims and product selection misinformation about use for medical conditions are problematic and not typically based on scientific studies.
 - Gray market products proliferating in states where there is not legalization or access to standardized cannabis material. This will continue to be an issue until there is standardization at the federal level in the U.S. This is a call to action that we urgently need regulation at the federal level of the U.S.

The Chair noted that while we are focusing on medical cannabis and intended use, the focus should be on quality standards because people using cannabis recreationally are often using products for some medical concern.

Industry Panel Questions

Q: How do you select and focus on specific plant pathogens and contaminants, and who should be in charge of contaminant testing?

A: Tjalling Erkelens: It must be up to industry in conjunction with regulators. Pharmacopeial monographs will steer the discussion on standards between industry and regulators. If using cannabis as a starting material, then genetic composition, chemical composition, and THC percentage is up to the producer and cultivator to align with regulatory requirements however, the basics of testing and growing conditions should be agreed on with the regulators.

A: Giovanni Appendino: Cannabis is not sterile. The issue is general for plant biomasses, especially from the tropics, because of toxins derived from contaminants such as aflatoxins. Cannabinoids are not shields protecting against biological contaminants.

Q: Does the definition of medical cannabis mean that it is smoked? The intended use for medical cannabis is as a drug; routes of administration can make a difference in terms of public health consequences for oral vs smoked/inhaled material.

A: Giovanni Appendino: Yes, that's a key point.

Q: We've heard a focus on genotypes, but there is confusion in the recreational marketplace about words used to describe cannabis plants. Is genotype a good predictor of phenotype and chemotype and how is this reflected in standardization?

A: Alan Sutton: We use the term chemotypes a lot because we produce with plant material chemically controlled beyond what is normally occurring in marketplace. (e.g., CBD, CBG, CBC) with the highest yield of cannabinoid in those plants. So chemotype refers to the plant's chemical profile. The genotype describes the individuals that belong to the chemotype.

Q: Chair: you're seeing consistent chemotypes?

A: Alan Sutton: Yes, we use a consistent profile year after year, which requires consistent growing environment from clones and is very well standardized.

Q: Chair: Theme of the event and session is standardization and harmonization. Question regarding botanicals with thousands of compounds that are difficult to standardize. The *Ph.Eur.* has a plus/minus 10% cannabinoid variance; but USP suggests plus/minus 20%, which one do we adhere to and how can it be resolved?

A: Tjalling Erkelens: German monograph has $\pm 10\%$; the European Medicines Agency (EMA) draft is expected early next year. And there is a big discussion on whether it should be $\pm 10\%$ or $\pm 20\%$. Should $\pm 10\%$ apply to medical or to the herb itself? We have had $\pm 20\%$ deviation in the Netherlands, the Dutch government is now moving to a level of $\pm 15\%$ and maybe down the road may be $\pm 10\%$ for the whole flower. USP sees it differently, so we need a discussion between USP and EMA on where this standard deviation should be on a global scale. Because we will see a global economy arise and need the same standards for that. My opinion is that the $\pm 20\%$ should apply to raw material, but when it comes to patients it should be in $\pm 10\%$ limit as for other medicines. This can be achieved.

A: Alan Sutton: Agree with that. We have $\pm 10\%$ for all APIs, finished products, etc., because that level of consistency is needed for patients. We do not supply botanical raw material (BRM) for patient use, but I agree if you use BRM (as the drug for patients) it should be consistent and you should know what you are getting.

A: Giovanni Appendino: Sampling is also an issue. You need fixed criteria for statistical sampling. Standardizing biomasses is more complex than standardizing extracts.

A: Tjalling Erkelens: yes, I agree with that. Another issue is the difference between the ways various laboratories sample and handle the samples. A good sampling and storage strategy agreed among labs is truly necessary to standardize the plant. I see big problems in the U.S. regarding influence of commercial cannabis on labs. Labs should be taken out of the commercial influence; we need government and regulators to step into that. And for patient use, you need good standards well overseen by regulators, and sampling is an issue and should be taken care of. There are differences in content between flowers of the same plant, not the profile, but the amount may differ. You need sampling protocols. And greenhouse and other indoor situations need strict protocols (e.g., time standardization, amounts of light, moisture).

A: Marcel Bonn-Miller: There are many different factors that impact THC percentage. And there are a lot of competing interests. How do you deal with that? There are issues ranging from time of drying to testing moisture content, all that impact THC reporting. We need to set minimum standards for quality parameters.

The Chair summarized the following themes and remaining questions:

- There are many different levels that need harmonization and standardization (e.g., how do you qualify testing labs?)
- Given that implementing good agricultural and collection practices (GACP) is expensive, how do you qualify suppliers?

A: Nandu Sarma: There is a detailed discussion in USP publication (<https://pubs.acs.org/doi/pdf/10.1021/acs.inatprod.9b01200>) about the inherent variability of cannabis and cannabinoids. While USP monographs for drug substances (such as pure compounds) have limits for content/assay of Not Less Than 98%, for certain matrices the range is wider, typically 90% to 110% for some of the botanical extracts because of natural variability. USP perspectives about the variability for cannabis-derived cannabinoids was shared with the EDQM (Ph. Eur.) for potential alignment.

Q: Chair: If you could get rid of a regulation that is troubling to your company or jurisdiction—or add one, what would it be?

A: Tjalling Erkelens: Take out treating cannabis as an opioid. Cannabis can be regulated properly. Bring in full standardization of cannabis, not just the level of THC and CBD.

A: Alan Sutton: It's a difference between regulatory bodies. Harmonization across countries would be useful. Noted a cannabis product licensed in 30 countries with clinical data, but not in the U.S. due to requirements around certain specific clinical testing.

A: Giovanni Appendino: Get cannabis out of schedule 1 drugs. Harmonize the regulations on synthetic and natural cannabinoids. Synthetic cannabinoids is an umbrella term.

A: Marcel Bonn-Miller: Wish is for federal legalization so that we can have consistent regulations.

David Vaillancourt emphasized the following:

- This panel talked about phyto-derived cannabinoids and the importance of characterizing the final products.
- Ranges are your friend when describing and characterizing your products.

Laboratory Panel and Discussion on Key Issues

Chair: Martin Woodbridge, PGC.PHC, DPH, MPH, Woodbridge Research

Martin Woodbridge provided a presentation on harmonization of cannabis quality standards for medical and scientific use. The presentation emphasized the following:

- Industry and regulatory authorities around the world are challenged by analytical inconsistencies (e.g., irregular lab practices, inconsistent analytical methods, variable quality reference materials and samples, variability in samples and sample preparations).
- Many laboratories across the globe are now required to both qualitatively and quantitatively identify cannabis and cannabis-derived products.
- The goal is to develop a globally adopted compliance-oriented monograph that considers cost, value, fit-for-purpose, and adoption by industry and global regulators.

Mahmoud ElSohly, Ph.D., University of Mississippi

Dr. Mahmoud ElSohly provided a presentation on insights into cannabis products quality. The presentation emphasized the following:

- University of Mississippi National Center for Natural Products Research participates in National Institute on Drug Abuse (NIDA) marijuana project activities related to growing,

harvesting, and processing cannabis plant material to produce standardized marijuana of different potencies for research (e.g., pharmacological studies, clinical trials, analysis of confiscated cannabis materials).

- Dr. Mahmoud ElSohly emphasized development and validation of a gas chromatography with flame ionization detection (GC-FID) method for the quantitation of 20 acidic and neutral cannabinoids in cannabis products.
- Our goal is to help in the standardization of the methods and qualitative/quantitative aspects of the different components of products on the market.
We are preparing a manuscript on the analytical method developed for the impurities in Δ^8 -THC products, which we have isolated and identified.

Chris Hudalla, Ph.D., ProVerde Labs, U.S.

Dr. Hudalla provided a presentation on consumer safety vs. regulatory requirements of analytical testing for the cannabis industry. The presentation emphasized the following:

- Cannabis safety is complicated by jurisdictional variance.
 - Contaminants to be evaluated and tolerance limits vary significantly.
- Challenges can be exacerbated by weak/ineffective regulations.
 - There are large variances in state requirements for product sampling, potency inflation, pesticide testing, and microbial contaminants.
- Black market poses multiple threats to the regulated cannabis industry.
 - Undercutting prices drives consumers to the unregulated market.
 - Absence of quality standards poses significant risk to consumer safety.
 - Prevalence of synthetic products on the market presents unknown hazards.
- Standardized methods and proficiency testing will help to address many challenges.
- Ultimate goal would be for global harmonization of standards.

Remco Vree Egberts, BAsC, Ofichem, the Netherlands

Dr. Egberts provided a presentation on the development, analysis, and production of APIs. The presentation emphasized the following:

- Ofichem's experience producing and challenges with analyzing medicinal cannabis.
- The Dutch OMC regulates medicinal cannabis in the Netherlands.
- Challenges in the analysis of cannabis include sample homogeneity, preparation (i.e., milling), microbiological examination (i.e., growth inhibition at lower levels), pesticides, and aflatoxins.
- Draft *Ph.Eur.* comments on the following needs more clarification:
 - Why is high-performance thin-layer chromatography (HPTLC) required?
 - Are microscopic tests required for each batch?
 - More descriptive information is needed regarding how to powder the material and appropriate procedures for sample preparation.
- The key takeaway is that a safe medicine starts with high-quality ingredients.

Chair (Martin Woodbridge)' summary: The European regulatory program and what quality standards are harmonized were described clearly and succinctly. Some important challenges were noted for labs (e.g., sample homogeneity, sample preparation, microbiological examination down to low levels, pesticide testing frameworks, and issues around introduction of new high-potency cannabis strains). Importantly, the *Ph.Eur.* Monograph was showcased, which is aiming for harmonization across the EU, and addressed some important questions on aspects of the monograph.

Gillian Schauer, Ph.D., MPH, Cannabis Regulators Association, U.S.

Dr. Schauer provided a presentation that emphasized the following:

- The challenge of terminology such as “medical” and “recreational” cannabis is that it is increasingly difficult to segment out these products and work toward safe use for both. Dr. Schauer prefers the term “adult use.”
- CANNRA exists to facilitate discussion amongst states about cannabis regulations, best practices, and differences across governmental programs regulating cannabis.
- CANNRA has been extremely active in discussing lab testing and consumer safety issues.
- States face a range of challenges related to lab testing.
- States vary in their testing approaches; these differences can require legislative action to change or modify.
- The current U.S. federal approach to hemp-derived products and novel cannabinoids poses a threat to consumer safety; regulations around lab testing are warranted.

Chair (Martin Woodbridge): You’ve provided a global case study of the challenges to achieving harmonization. You identified current problems finding appropriate terminology the markets and industries use. It is important to reinforce the message, are we all talking about the same thing? Reference labs are a big challenge, especially the ability to cross-validate across states. There is a direct need for a state reference lab. One with leadership across the states is an important component. And the need for effective and competent and well-resourced regulatory authorities who can do audits and provide oversight for highly functioning industries and markets. Finally, it was pointed out that politics might come before science and good practice.

Laboratory Panel Questions

Q: There are reports of laboratory-to-laboratory variability in results, lab shopping for results, inappropriate sampling selection or preparation, and inconsistent testing for contaminants. What are the biggest challenges to harmonization?

A: Remco Vree Egberts: Sample taking and sample selection at the producer level is step one. It has to be a homogenized sample to start with to reflect the batch. Second, sample prep in the lab has shown big differences. I think it should be better described in an appropriate way for consistency among laboratories.

Q: About pesticides and testing, what is an appropriate risk-based approach where we identify a number of potential samples, and should we be screening or something in-between?

A: Chris Hudalla: It’s something in-between. Cannabis as a natural product is inherently inhomogeneous. We have seen top and bottom flowers from the same plant differ in cannabinoid potency by as much as 50%. When cultivating outdoors, there are challenges around pesticides, microbes, and residual solvents because these contaminants can be equally inhomogeneous in their concentration throughout the matrix.

Q: Do we need more regulatory criteria for entry sample collection and submission of those samples, or more minimal requirements around certification and quality, or valid uniform certificate of analysis issued by the lab? Any thoughts on those topics and their relevance from a regulatory perspective?

A: Gillian Schauer: One of the challenges is that every state has their own third-party lab testing system. There are a small number of bad actors that make this very challenging for regulators. Sampling and sampling testing are big pieces of it. In an ideal world, we would likely have a neutral party get the sample and deliver it to a third-party lab. Enforcement is challenging

because regulatory agencies are generally understaffed on scientists who can help labs in ways that are needed. And they don't have access to state testing labs to be able to help validate testing methods and arbitrate lab-to-lab differences. However, states are introducing approaches to deal with round-robin use of labs and periodic spot checks. States are working hard to make improvements.

Q: Does laboratory certification actually work in the medical and scientific field with cannabis? Are ISO Good Laboratory Practices (GLPs), GMPs, or something else appropriate?

A: Gillian Schauer: From talking with state scientists, I think that the consensus is that ISO 17025 is an absolute minimum and heard that there were changes in the 2017 version that may have made things more challenging as a bare minimum.

A: Chris Hudalla: you want to stay as current as possible, so the 2017 version is the standard for labs now. The ISO 17025 is a minimum requirement. I don't know as much about others but I think they should be similar. Accreditation is critical. It is a driver's license; it doesn't mean you're not going to speed.

A: Remco Vree Egberts: In Europe, regarding medicinal cannabis, you need GLP and GMP for medicines for the market. These companies, in the Netherlands, are controlled by the authorities and you will be audited by the Dutch Ministry of Health for that. For medicinal cannabis, it's another issue related to the different regulations between different countries.

Martin Woodbridge: It comes down to harmonization, which is the key being discussed today.

Final Wrap Up

Q: David Vaillencourt: What are your reflections from these sessions and what do you consider to be the three top issues?

A: Holly Johnson: We may be closer to harmonization than we think in some ways with product quality. Going forward may be with an evaluation of existing monographs to review their differences (e.g., plus or minus 10% or 20% for certain materials). For monographs and standards, we may be closer than we think.

Among the common themes that I heard: the patchwork of regulations in the U.S. is modeled by the global situation. In some ways it is the legal/regulatory situations that have led to quality and testing issues. We are close in some ways, but we still have a patchwork in regulatory concerns. I urge regulators, legislators, and advocates to contact scientists and ask for suggestions and share data and make suggestions before regulatory/legislative language is enshrined in a way that's difficult for us to interpret.

A: Gillian Schauer: U.S. can serve as a microcosm for what can happen globally, and it is somewhat worrisome. I'm curious to hear from other speakers how they think we'll reach global standards. Some may be easy when we have well-validated, scientifically developed official standards for certain areas of lab testing, which are more likely to be widely adopted. But for a lot of these other things where there's gray area, how do we get there? We're struggling just in the U.S. It has been a challenge for years.

A: Andrew Wayne: For approved drugs and therapeutic products, there will be alignment because there's an existing framework and mutual recognition of GMPs. However, a lot of cannabis producers just produce cannabis without having to undergo the safety and efficacy trials. Is it appropriate to apply pharmaceutical standards to something that's not a pharmaceutical and not a therapeutic product, especially in jurisdictions like Canada where there's an adult-use stream? Do we hold cannabis to quality standards except when it's a drug, in which case the GMPs come in? Maybe that's an existential question in conversation but one that I think about as a regulator.

A: Robin J. Marles: The gold standard for regulations does not exist. Canada has had a framework in place for some time but we have our challenges as well so one of the encouraging things is looking not only at where we can harmonize, converge, or align, but also complementarity. We cannot possibly cover in a *USP* monograph or *Ph.Eur.* monograph all the aspects that need to be dealt with to ensure quality and that's where other standards organizations like ASTM can contribute to the global package of what is needed in this area.

A: Tjalling Erkelens: Although it will be very difficult in North America, the separation of recreational and medicinal use of cannabis would be key. Canada and the U.S. have chosen to leave cannabis out of the pharmaceutical environment, basically creating a separate system. I plea for regulatory systems that can allow cannabis into the pharmaceutical space under high-level regulations as is happening in Europe. The main point is that if you send patients to the recreational market, you are turning your back on them from a regulatory point of view. The recreational user wants something totally different than patients, most of whom do not want to get high on cannabis. Recreational users are looking mainly for that mainly and that already separates the markets. If we cannot do that, we keep creating problems.

One of the most urgent needs right now is to separate the two regulatory worlds comprising 1) a medicinal market that can be truly monitored by the regulator in an organized way and 2) the recreational market where we have a different set of requirements for consumers. It is a bold step to create two worlds, but from a patient and medicinal perspective, if we look at the scientific evidence of cannabinoids and their value as a medicinal product we need to separate the two worlds. For that purpose, these two days have helped us understand that. We need more discussion between the U.S. and Europe especially. Asia will come up within the next few years and require regulations.

A: Martin Woodbridge: Cannabis inflorescence and leaves are the building block of industry and cannabis medicines, so it seems sensible to the focus our attention there initially for harmonization. And if we do have the global monograph, the value and global acceptance will be key. The second point is that regulators need to be well equipped to perform the tests they need to do within this industry so we can have quality monographs and regulators that are able to audit and detect the needs of laboratory-related issues.

A: Nandu Sarma: There are resources available to address many of the topics raised in this workshop. While there are differences, there are frameworks for bringing the different groups together. We need to continue the conversation.

A: Gillian Schauer: I appreciate that we need to bring regulators into the conversation because they help to implement the standards and look at the feasibility of different standards in the real world, which is of critical importance.

A: David Vaillencourt: This workshop is the start of conversation. Sampling is complex with many technical aspects and details. No one industry group or state, federal, or international regulatory group can really solve all the issues. It is important to call scientists for valuable information to work together across disciplines. The word convergence stuck with me as we work through alignment and convergence. We can strive for harmonization and improvement through data sharing and conversation and we can get to a more convergent marketplace where consumer safety is the forefront. We need to have a conversation and identify the problems before we can start solving them.

A: Robin J. Marles: From a Canadian perspective, our federal acts and regulations are designed to be complementary. This is an area where we have not excluded the drug aspects of pure cannabinoids. We haven't closed that door. As further products are developed to the level of drug quality, and clinical trial work is developed, there will be a channel for high quality, highly standardized products for medicinal purposes.

A: Andrew Wayne: if you want to do clinical trials you have to do that with GMP material. Very few have gone that route. The majority are going Good Production Practices (GPP) route with no health claims. Health Canada just introduced a new set of regulations to allow clinical studies

for nontherapeutic purposes to occur for GPP cannabis. Those regulations went into effect. That's an example of a different set of standards providing a big hurdle for researchers. People wanted to do trials but could not get access to GMP cannabis products and needed a new regulatory framework to address that. So, standards can be a real solution for people as well.

Dr. Sarma thanked everyone who participated in the meeting and who organized and handled the logistics of the workshop. This was a wonderful example of how organizations can come together and facilitate a conversation. Some were unable to be at the table due to logistics but when we go to the deep dive conversations we will need all of the relevant players to provide input. We heard from regulators, standards organizations, and laboratories on three continents about their experiences, challenges, and available resources, which provide hope for a forum and having a conversation on science-based approach so we can talk the same language and likely come to mutually acceptable agreements. This conversation will continue, so please stay engaged. There's more to come.