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# A sea change at National Harbor? Excerpts from IPEC-Americas' Excipient World Conference.

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Opinion and Commentary

## ABSTRACT

When it comes to achieving good return on investment for a conference there are three important elements: the quality of the program content; the quality of the presenters; and the quality of the attendees. All these factors ranked very high for the Excipient World Conference (EW25), that took place from May 12-14, in National Harbor, MD. More than 200 attendees participated in the meeting with representation from excipient developers/suppliers, pharma/biotech/veterinary medicine, academic institutions, and both the USP and the FDA.

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When it comes to achieving good return on investment for a conference there are three important elements: the quality of the program content; the quality of the presenters; and the quality of the attendees. All these factors ranked very high for the Excipient World Conference (EW25), that took place from May 12-14, in National Harbor, MD. More than 200 attendees participated in the meeting with representation from excipient developers/suppliers, pharma/biotech/veterinary medicine, academic institutions, and both the USP and the FDA. The organizers, IPEC- Americas, did an outstanding job building the program around a combination of interactive workshops, educational talks, and expert roundtables. Throughout the conference numerous networking sessions fostered interactions between the guests to build great connectivity in this vibrant community of experts and experience. There was also an excellent poster session that included more entries than previous years with topics ranging from drug delivery (such as a study on the use of DMSO for skin delivery of fluconazole); excipient roles in biologics formulations (evaluation of polysorbate grades on monoclonal antibody formulation stability); outputs from workstreams (e.g., an update on ethylene glycol and diethylene glycol), effects of excipients on oral product performance (e.g. influence of antioxidants on tablet dissolution and implications for biowaivers) and discovery of novel materials (design of a blocker of bitter taste receptors designed to improve the taste of therapeutics.)

The theme for the meeting "The Changing Landscape: Positioning Excipients for the Future, was never more apparent than during the parallel workshops that opened the main program. Professors Jim Polli (University of Maryland) and Stephen Hoag (University of Maryland) and Priscilla Zawislak (IPEC-Americas/Roquette), led a session focused on the essentials of dosage form development for more conventional small molecule therapeutics. As a complete contrast, the other parallel session was a Biologics Summit focused on cell and gene-based therapeutics. This session was conducted in conjunction with members of the Controlled Release Society and is part 1 of an ongoing program. (N.B., the second part of the series will be presented during the CRS Annual Meeting and Exposition, July 14-18 in Philadelphia.) The rest of EW25 covered a diverse collection of excipient topics including current trends and challenges, latest innovations, and glimpses into the future for excipients and their ubiquitous roles for the healthcare and associated industries. Given the richness and depth of many of the sessions it is not possible to give a detailed account of the content, but the following are some of the key takeaways from various sessions:

The opening session of the Biologics Summit was focused on an introduction to cell and gene therapy and was presented by Basak Clements, Biomatria Consulting, LLC. The ability of biotherapeutics to profoundly impact human health has been evident through the rapid introduction and adoption of monoclonal antibody (mAb) products. Since the first introduction of mAbs in the mid-seventies, the market for mAb products has increased dramatically to reach $250B in 2024. In comparison, having been conceptualized in the early seventies, the first gene therapies were approved/introduced in 2017 (e.g., Luxturna) and only about 17 cell therapies have been approved worldwide to date. Last year FDA approved a record 8 cell and gene therapies with 20 such products being approved over the last three years. Gene therapy delivers genetic material, such as a working gene, to modify how a protein is produced by a cell. Genetic material is delivered by a vector that can be viral or non-viral in nature. The latter are less expensive and allow repeat dosing with fewer immune issues but are less efficient and are more difficult to use for *in vivo* gene therapy due to targeting challenges. Marketed products include: Beqvez (Adeno-Associated Virus vector, AAV), Imlygic (Herpes Simplex Virus type 1, HSV vector), and Elevidys (AAV). Cell therapies can be regarded as a type of gene therapy in which specific cells are modified with genetic material. Marketed products include Breyanzi and Yescarta. Cell therapies are classified as either autologous (such as Kymriah); in which the patient donates their cells to be modified and administered back into their body, or allogenic; in which cells come from healthy donors (such as Cartistem.) Excipient roles in this area include use of DMSO as a component of the cryopreservation treatment for the cells, and lipid nanoparticles that are being used, along with polymers, for protection, targeting and delivery of genetic material.

The influence of DMSO as a cryoprotective agent was reported in more detail in a presentation by Sarah

Poynter, Wilfrid Laurier University, Canada. In her talk Dr Poynter described how DMSO prevents ice crystal formation and penetrates cells to decrease the osmotic stress during the cryopreservation process that involves freezing to minus 80ºC or, more effectively to minus 196ºC with liquid nitrogen. Typically, a concentration of 5-10% DMSO is used in this process, with the DMSO being removed after thawing of cell samples. Using cell culture, Dr Poynter's team investigated the effect of DMSO purity on the viability of cells undergoing the freeze-thaw process. Different DMSO purity levels from 99.7% to 99.99% were tested in cytotoxicity assays involving various murine and human cell lines with alamarBlue as a marker for cell viability. Results from these studies demonstrated a marked increase in cell viability post thaw (~20% improvement) with a high purity DMSO (Propicient, min. 99.99% pure) versus other, less pure, DMSO samples. This difference was somewhat dependent on the cell line being tested and work is continuing to determine the implications of this work to other cell types.

Excipient importance to lipid nanoparticle delivery of mRNA vaccines was showcased by Magali Hickey, Stealth Biotech PBC (and Örn Almarsson, Axelyf). Lipid materials are present in much greater amounts (milligrams) in such vaccines compared to the RNA which, for potent vaccines, is tens of micrograms. The presentation outlined how excipients play crucial roles in various products such as SpikeVax. Ionizable lipids and PEGs have been used in commercialized RNAi products such as Onpattro, approved in 2018. Lipid nanoparticles (LNPs) are effective delivery systems for RNA-based therapeutics and in such formulations the excipient components: ionizable lipid, phospholipid, sterol, and PEG lipid play critical roles in the performance of the product by influencing delivery of the RNAi to the target site, retaining at the site for as long as possible, and for accelerating its removal from the body as soon as the active has done its job. Low bioburden is an essential requirement for all excipients during the fabrication of LNPs using multi-step, aseptic processing. An example of Critical Quality Attributes (CQAs) was outlined for LNPs including size, polydispersity, surface charge, etc. Such an example is illustrative, but each product needs to have its own set of attributes defined and then met. Several novel ionic lipid excipients have been developed and some are produced at the requisite purity, in larger quantities these days e.g., ALC-315 (Comirnaty) and SM-102 (SpikeVax, mRESVIA). mRNAs are large and labile biomolecules that are difficult to develop as products for the reasons given above and because they currently require cold chain storage strategies. This, and the other various challenges, represent increasingly important opportunities for novel excipients to increase their roles in development of more effective and more robust lipid nanoparticle formulations for future mRNA vaccines and therapeutics. Several recent publications provide additional information on this topic see (1,2).

The increasing relevance of excipients to development of new therapeutics was recognized in USP's perspectives on new frontiers in excipient qualification and development, presented by Catherine Sheehan, USP. USP has made significant efforts to develop alternative processes, new tools, and resources to facilitate excipient developments for the pharma and biotech industry. Several valuable initiatives have been undertaken by USP including, but not limited to:

**USP Emerging Standards program —** an Emerging Standard (ES) is a potential standard for a material in its initial development phase that is shared with the community to encourage dialogue. ESs are not official USP standards. The objective is to help influence what the future potential standard could look like.

**USP Materials program —** that includes USP Analytical Reference Materials (ARMs) launched in response to stakeholder feedback based on market needs. New ARMs are released on a rolling basis to address novel and evolving industry needs for drug development and analytical testing.

**Complex excipients used in complex injectables —** A priority in the USP Science-Excipient Strategy with a focus on development of standards and solutions for lipid compounds. These excipients can significantly impact liposomal formulations (and by extension, LNPs) as well as consistency in batch-to-batch performance.

**Novel Excipients —** USP is actively engaged in developing greater awareness and resources to facilitate new materials with positive benefits for product development and, ultimately, provision of new therapies for patients. Several initiatives have been established to facilitate knowledge exchange such as USP's Novel Excipients Expert Panel (that includes toxicologists from around the globe, constituted to update USPs General Chapter *"Excipient biological Safety Evaluation Guidelines"* <1074>); use of the ES concept and Analytical Reference Materials (ARM) approach; and creation of the USP Novel Excipients Knowledge Hub. USP was also involved in FDAs PRIME program.

Given the impact excipients can have on products there are some commercial considerations (such as IP) in sharing of information in the "public domain", such as with USP. To address this concern USP has developed confidentiality agreements/non-disclosure documentation to protect information provided by third parties. Additional information on these initiatives and other topics was provided by USP through the course of the event including a comment that precedence of use from the IID is necessary for an excipient to be on the NF and USP encourages interaction with them once IID precedence is established to initiate a monograph.

A pediatric workshop was conducted by: Smita Salunke, UCL School of Pharmacy; Kevin Hughes, Colorcon Ltd; April Braddy, US FDA; Seiji Takae, JPED/Astellas. The objective of this workshop was to provide attendees with knowledge and tools necessary to evaluate several pediatric formulation challenges and propose suitable strategies to overcome various issues relevant to development of these unique products. Children represent a very diverse patient group and should not be regarded as small adults as their physiology and ability to accept certain dosage forms can be very different from adults, as can their ability to tolerate certain doses of excipients and medications. Pediatric products typically represent much lower sales volumes, and clinical trials have been notoriously difficult to conduct, which resulted in limited investments to develop these products in earlier years. This paucity of suitable pediatric products resulted in various agencies introducing regulatory requirements such as the pediatric study plan (PSP) in the US, and in the European Union (EU) the Pediatric Investigation Plan (PIP) process designed to ensure pediatric developments are undertaken for all new products unless the nature of the therapeutic would not have an application in children. This process has been adopted widely and applications over the years have highlighted the limitations on excipient use in this patient population. A publication by Ruiz (3) described an analysis of proposed PIPs in which excipient issues were cited for a significant number of the dosage forms proposed for children. The excipient selection conundrum is that there is no regulatory list for excipients suitable for use in pediatrics. While there is guidance on points to consider when evaluating a material there is often very minimal information that is available to help determine/justify the suitability of a given excipient. Some useful sources are the Safety & Toxicity of Excipients for Pediatrics (STEP) database (4), an open, curated source of toxicology information for ~75 excipients; the Japanese Pharmaceutical Excipient Directory (JPED) that contains information on >1440 excipients used in pharmaceutical manufacturing in Japan; and the Pediatric Excipient Risk Assessment (PERA) tool for assessing potential products for use in pediatric populations (5). The objective is to use a science-based risk-benefit analysis of the desired product/formulation, and to identify any possible issues in using it for a specific pediatric application. PERA represents a summary of information that has been identified to date and it is by no means an exhaustive list. To be used effectively it needs to be supplemented with published literature and data in FDA's Inactive Ingredients Database (IID). In response to questions, a member of the FDA shared information that the agency started to collect data for a pediatric "IID" in 2021. This "prototype development" has not been released and there are no immediate plans to do so but with increased industry lobbying it might be possible to do something more official with this alleged nascent effort. Other potential reference sources for supporting choices of excipients for pediatric formulations include the Electronic Medicines Compendium and information from any precedence of use in other countries. While this approach can be beneficial, caution is needed because interpretation of available data can vary between agencies based on the differences in country-specific patient populations.

Public scrutiny of various excipients used in foods, etc., has led to bans on various artificial colors, etc. Such actions exert pressure on other industries, including pharmaceuticals, to consider similar restrictions on the use of certain materials. In a summary spotlight presentation Ted Sullivan, IPEC Americas' legal counsel, described differences between Federal vs State legislature practices and the potential implications they have for development of products for multi-state distribution.

This complex situation is evolving, and IPEC-Americas is constantly working to understand all the main issues affecting excipients and how to influence outcomes in conjunction with its members and partners.

A roundtable session involving key stakeholders focused on insights for introduction of new excipients. Meera Raghuram, Lubrizol, explained that, given the extensive range of applications for excipients, there is enormous potential to create new materials offering improvements over existing products. Embarking on new excipient innovations requires careful consideration of financial, legal, and regulatory aspects, to name a few. A more straightforward approach is the development of new grades of existing materials (with no change in chemistry) to fulfil a client request/market demand. A bridging justification based on available information may be sufficient to support the introduction of such a product. Literature should be evaluated, and the risk assessed to determine whether this will be adequate, or whether additional safety data should be generated to supplement any application. It is important to note that the maximum daily exposure listed in the FDA's IID is the highest level of an excipient that has been used in an *approved product*. This may not be the highest level that has been tested in safety studies and data might be available from other sources that can be cited to support an application for a new level, use, etc., for an excipient.

Anticipation of requirements for new excipients was further exemplified by David Schoneker, Black Diamond Regulatory Consulting LLC, who described efforts to develop various decision trees to cover different use cases for new excipient developments. The presentation was based on a hierarchy of these use cases ranging from new excipient grades with no chemical change through a new excipient with minor chemistry changes, and to most challenging case of novel excipients. Key points in the discussion were the importance of "context of use" which defines why something matters or applies in your specific intended use. It is not sufficient to rely on the fact that your application is based on the excipient being below the IID limit, this must be put into context with your intended use to make sure that it is a limit based on the same administration route, etc. The same philosophy applies to leveraging GRAS information to support new excipient use. GRAS is used by the food industry primarily and it relates to oral administration where it can provide valuable bridging justification for oral medications, but this is unlikely to be useful for an excipient being pursued for intravenous formulation. Panelists recommended that any customers employing a new excipient in their product must build a close partnership (vs a transactional relationship) with the supplier to jointly generate the relevant data package and to minimize risks at submission. A key next step proposed by the group was to build a strong coalition to advance the science and framework for new excipient products because innovation continues in our industry and there is a gap in guidance to makers and users. Furthermore, work should begin on the development of a guide outlining the regulatory strategy and the issues related to new excipient product development. Interested parties are welcome to participate.

Sudhakar Voruganti, Pfanstiel, described market drivers for high dose subcutaneous (SQ) formulations for IgG monoclonal antibodies (for various formats see (6)) and introduction of arginine glutamate as a novel excipient for this purpose. According to Adler et al., (7) 41% of mAb products approved between 2015-2023 were administered by SQ injection compared to 24% between 1994-2014. The limited dose volume via the SQ route has resulted in marketed high concentration (≥ 100mg/ml) low volume (1-3ml) (HC) SQ formulations (e.g., Nucala®, Emgality®), with some products at much higher concentration (200mg/ml, e.g., Benlysta®), or products administered SC in much large volumes by incorporating a hyaluronidase drug delivery component into the formulation (Herceptin Hylecta®, Tecentriq Hybreza®). High concentration SQ formulations pose numerous challenges to formulators including aggregation, low solubility of proteins at high concentration, liquid to liquid phase separation, and increased viscosity that makes injection difficult. For a review of formulations of commercially available antibody products see (8). Platform antibody formulations typically include buffers (phosphate, citrate, etc.), sugars (such as trehalose, sucrose) and surfactants (polysorbates) with a final solution pH in the range 5-6.5. Excipients play important contributions to product viability for instance by producing viscosity lowering effects, typically achieved through addition of amino acids (e.g., glycine and arginine). Arginine hydrochloride, a protein aggregation suppressor, has been shown to decrease viscosity (9) up to about 6-fold when added at concentrations of 150-450mM to a 250mg/mL antibody solution (10). There are also reports of such amino acids significantly increasing protein solubility by more than 8 times (11). Arginine glutamate has been launched as a GMP grade and suppliers regard this as a promising alternative excipient for consideration as a viscosity-lowering agent in high concentration SQ monoclonal antibody formulations. It has been shown to reduce aggregation propensity for mAbs in solution as demonstrated under accelerated stability conditions (12) at concentrations below 200mM to ensure clinically acceptable osmolarity. Other potential benefits demonstrated with arginine glutamate include improving thermal stability (protection of CH2 domain in the mAb) and reducing visible liquid-liquid phase separation. This material represents a useful alternative excipient for use in mAb SQ formulations that continue to be in high demand.

In a divergence from human therapeutics the presentation from David Medina, Pet Flavors, outlined current trends in pet care which is an expanding market due to the "humanization of pets" and the rising prevalence of chronic conditions in companion animals, and commensurate medications to maintain their lifespan. Injectables are the most popular products (47% market share) with oral products coming in at second most popular (37%). Like human therapeutics, safety and efficacy are paramount to companion animal product viability and performance. For oral treatments in pet care there is another element that is essential for product effectiveness — acceptance by the animal. Palatability is key and there are various aspects to this in terms of taste, swallowability (including size, shape, and texture of dosage form,) etc. The EMA criteria for products to be palatable are: ≥80% acceptance for dogs, 70% acceptance for all other species. Advances in formulation technology, especially development of novel flavoring agents, are anticipated growth areas as pet care continues to improve as owners increasingly treat their pets as family members and demand premium ingredients and best treatments. In addition to more standard considerations (providing COA's, safety data in SDSs), provision of flavor excipient stability data (for 3-5 years), and excipient particle size control on every production batch, are important considerations in selecting a supplier for companion animal product development.

A more detailed exposition on drug palatability was provided by Fernanda Onofre, dsm-firmenich, in her presentation on exploiting knowledge of sensory receptors to develop taste modifiers. More than 60% of APIs are considered bitter which highlights the potential for better taste science in development of oral liquids for instance. Humans have five basic tastes (sweet, umami, salty, sour, and bitter) that are detected by various types of taste receptors located across the tongue. Very little has been reported on the structure of most of these receptor types. Importantly, unlike other tastes that have only one receptor type each (sweet and umami), there are 25 different bitter receptors (TAS2Rs). The same receptor can be mutated between individuals which makes taste perception extremely complex. In addition, multiple ligands may bind to one receptor, multiple receptors might bind one ligand, and a molecule can act as both a receptor agonist and antagonist. These different properties and behaviors of both the physiology and chemistry make the science of modulating bitterness very complicated and challenging. Using a cell-based assay utilizing taste receptors expressed in cell culture, compounds can be screened for their ability to block bitterness. In one example, a candidate was identified (S9932) that was able to block the TAS2R39 receptor, a bitter receptor activated by acetaminophen. This lead candidate, S9932, (at 50ppm) significantly reduced the bitter taste of acetaminophen (90mM) in a sensory evaluation test in humans. The goal is to advance bitter taste receptor antagonists into further development as putative alternatives to currently available approaches for improving product palatability. It is important to note that bitter blockers should only be considered as one component of a flavor that typically have dozens of ingredients including: carriers, modulators (taste boosters or maskers, as well as blockers), sensates (that provide sensations such as cooling and tingling), etc. All these elements must be used in combination to achieve more sophisticated taste modification.

Sustainability continues to be of great importance and relevance in our industries and Jeffery Richards, Alnylam Pharmaceuticals, provided an informative account of how Alnylam is leveraging AI technology for sustainable supply chains. The company is young (founded in 2002) and started to integrate sustainability from the beginning to avoid time, effort, and costly changes in business practices later on. Sustainability must align with business objectives for long term success and the vision for it should be conveyed to both internal and external stakeholders to maximize the probability of success.

The presentation described in detail the complexities in advancing a robust sustainability program in an environment that includes many hundreds of external suppliers. The approach adopted was to use technology and AI to turn sustainability "from a burden to an opportunity" by allowing automated data collection; AI powered knowledge bases; enhanced training for suppliers; a centralized marketplace, and AI-driven decision making. A third party provided the AI technology that enabled a more proactive approach for data management and evaluation. A key benefit is that AI platform provides an ability to view information daily versus storing information in spreadsheets that are typically reviewed infrequently.

Misconceptions surrounding co-processed excipients were discussed by Joseph Zeleznik, IMCD US. Co-processing of materials stems from work in the mid-last century by the food industry to enhance texture and flavor in food. These days co-processed excipients are available that are highly functional and offer significant benefits for oral dosage form manufacture. Of the 128 co-processed excipients identified in patents, the majority are binary mixtures (77%). Most common materials used are microcrystalline and powdered cellulose (39%) and lactose (32%). Co-spray drying is the most common method for production of co-processed excipients. There are numerous definitions available to delineate co-processed excipients versus binary mixtures of materials. IPEC defines co-processed excipients as "a combination of two or more compendial or non-compendial excipients with varying composition designed to physically modify the functional properties, not achieved by physical mixing and without causing a significant chemical change". USP states that co-processed excipients must be distinguishable (measurable) in at least one non-performance-related attribute from the corresponding physical admixture with no formation of a covalently bonded entity". Co-processing typically involves incorporation of one excipient into the particle of another to create integrated, engineered particles, each particle being of near identical composition. These "engineered particles" are not easily separable at the particle level. Co-processed excipients (CoPEs) offer several benefits for oral dosage forms such as: improved flow, better compaction properties, improved film formation, greater hydration, stability enhancement, and rheology modification. Regulatory agencies are not harmonized in how they regard co-processed materials and whether they are "novel" excipients. CoPEs are uniquely different than the parent ingredients but if there are no chemical changes they shouldn't be regarded as novel excipients. FDA and Japan authorities have similar views on CoPEs but until quite recently the EU agencies initially treated them as drug product intermediates, without the active substance. More recently, the EMA published a Q&A document (July 2024) stating that a co-processed excipient "is not a novel excipient" and "is not a finished product intermediate without active substance", and a CoPE is not a "ready-to-use mixture" as referenced in EU Guidelines. While these changes indicate greater appreciation of what co-processed materials represent, a few requirements/discrepancies remain such as one proposed requirement for the expected use of purified water for CoPE manufacture. This grade of water is not necessary for standard excipients and it would require an extraordinary amount of purified water to meet anticipated CoPE manufacturing demand. IPEC has submitted comments to EMA regarding the Q&A document and is currently developing a position paper concerning CoPEs to clarify certain points that have been misunderstood by EMA and some others. These important materials represent an opportunity to develop "tailor-made" excipients with exquisitely precise functional properties that could facilitate the advancement of valuable manufacturing processes such as continuous manufacture. N.B. Anyone reading this is referred to a previous issue of this journal that contains an article on co-processed excipients written by Joe Zeleznik and his colleagues (13).

Recognizing the international aspects of the conference, the last roundtable on day 2 focused on European decisions impacting excipients. Several areas of interest were highlighted from microplastics through to titanium dioxide. Some of these topics were discussed in an anticipatory manner, for instance, microplastic requirements in the EU, and some recent activities associated with "atypical actives". These themes will likely be considered by certain IPEC working groups to assess the possible impact of these topics to excipients. For instance, medicinal products are currently derogated from EU restrictions on microplastics although excipient makers and users are subject to certain reporting and labelling requirements from May 2027. The precise details of the derogations and their applicability are still to be determined and this topic requires a concerted industry effort to proactively assess the implications. More definitive information was possible for discussion of nitrosamines and titanium dioxide. Nitrosamines have been identified as carcinogenic and there are limits on their presence in drug products. Based on available information, only one excipient is known to contain any nitrosamines. In other words, in most cases the root cause of nitrosamines in a drug product is not because excipients have introduced these materials into the formulation. Excipients may contain nitrites that are inherent in their composition and can be extremely difficult to remove. The presence of nitrites could result in nitrosamine formation through interaction with other components in the drug product. The limited information available makes it difficult to determine the best way forward with this matter. Some suppliers are attempting to reduce the presence of nitrites in their products to reduce the risk of nitrosamine formation, but it is not clear on how much impact this will have. Similarly, there are uncertainties on which analytical method should be adopted to characterize nitrite levels. Some methods have been developed and are being published but more work is required in the area.

Raising the topic of titanium dioxide, $TiO_2$, David Schoneker, Black Diamond Regulatory Consulting LLC, stated that there are no safety concerns with this material from an excipient perspective. He asserted that EU comments have been misconstrued because these comments were related to nanogrades not having the full data package and these grades are not used in foods and medicines. Despite this, it has led to a EU ban of titanium dioxide in foods (2021). The EMA has taken three years to gather information to understand the possible impact of this ban being applied to pharmaceuticals and a readout is expected this year. It seems incongruous to think that this ban would be realistic given that apparently 91,000 drug products marketed in Europe contain this excipient and these would all need to be reformulated if there was a ban. Importantly, no other major regulatory agency in the RoW has supported the EU position and they have stated that $TiO_2$ is safe. In addition, Japan's Pharmaceuticals and Medical Devices Agency (PDMA) apparently conducted a study with 6 nanometer titanium dioxide and found no genotoxicity concerns. There are a few countries which follow Europe (primarily in the Middle East), that have banned $TiO_2$ but they may reconsider their position now that JECFA have done their evaluation and found $TiO_2$ to be safe for food uses, with an ADI of "not specified". As stated in an earlier session of the meeting, these actions by regulatory bodies do not preclude US states from making their own designations and titanium dioxide has appeared in certain State bills. This is clearly a topic that requires continuous vigilance by the industry to avoid unnecessary, and potentially devastating consequences to drug product availability to patients. This matter has potential ramifications for other excipients that are nanosized (such as iron oxide, magnesium stearate) and could also fall under scrutiny. This is already under consideration in some countries.

In the guest plenary session, Dr Andrea Love posed the intriguing question: "Can excipients bridge the science misinformation gap?" Misinformation and disinformation (where false information is spread intentionally) represent an existential threat to global science. There are various motivations for such activities that are encouraged and amplified through social media channels. A survey conducted in 2021 reported that 71% of Americans get their "news" from social media content. Even more alarming data points are that false information is transmitted 6 times faster than facts and that although only 28% of Americans have civic science certification, 52% of adults in the country consider themselves interested in issues involving science and technology. The discrepancy in knowledge versus interest is constantly exploited by people intent on creating misleading and erroneous claims about healthcare. The ubiquitous use of excipients in foods, pharmaceuticals, nutraceuticals, makes excipients uniquely positioned to positively influence public opinion of their value, etc., but it also represents a significant risk to these materials being the subject of misinformation. Minimizing this risk requires continuous awareness and a more coordinated, systematic approach to proactively influence opinions in advance of circulation of misleading social media posts, and to engender more understanding and knowledge in the public so there is a greater appreciation of what is misinformation and what is not. Dr Love shared examples of using her CRABS framework that is a simple but effective tool for identifying misinformation:

**C**onflict of interest — who or what conducted the study & what do they gain from it?

**R**eproducibility – is there other evidence in the field or is this a one-off study?

**A**uthority – are the authors qualified in the field?

**B**ias – Are the results reported appropriately? Is there any HARKing – hypothesizing after results are known?

**S**ource – where is the work published, is it in a peer reviewed journal?

CRABS is recommended to help manage situations where excipients are being targeted unfairly, to dismantle pseudoscientific claims and to guide communications with the public and regulators. The goal is to justify decisions based on evidence, not consumer pressure, to reassure others by applying the data, knowledge, and expertise available in our industry that is typically unseen and disregarded. This is an exceedingly difficult task that requires changes in our behavior to represent science in a more accessible way because currently the complexity of legitimate science is no match for the simplicity of misinformation. Teaching tools proposed included: Ingredient visual aids, myth busting (debunking) templates comparing fact with fiction (with simple language e.g., use of the term "chemicals" rather than "excipients" which is a poorly understood term), providing educational workshops/webinars to schools and universities to explain the healthcare industry and how excipients are involved, etc. Our industry should adopt a more anticipatory approach and be ready to "pre-bunk" any emerging efforts to generate the next "excipient scapegoat". Explaining why excipients are included in drug products, and what the consequences would be without them, needs more communication and reinforcement to reduce the impact of any misinformation efforts that will inevitably continue to be advanced by those intent on creating negative opinion in the public domain. Science is also threatened by misinformation due to the recent expansion of digital publishing and the increased presence of predatory journals some of which have minimal or no scientific review before publication. We are in the fortunate position that our excipient community can publish in this journal, the International Journal of Pharmaceutical Excipients, that is peer reviewed by an outstanding Scientific Review Board, constituted with accomplished scientists with experience and expertise relevant to our business. This journal represents a valuable way we can all leverage our wherewithal to highlight the outstanding science underpinning our industry and to represent it in an appropriate manner. In summary, misinformation is a systemic threat to our community that requires a rethink on how we communicate to the external environment through pre-bunking, public-accessible information, education through webinars, and publishing science in the IJPE, etc., to develop greater understanding and advocacy in successive generations. Dr Love is a highly engaged and engaging scientist with a passion to eliminate scientific misinformation. If you are interested in this topic and her aspirations, I highly recommend you consider exploring the content on her website (14).

In what is always a much-anticipated session, Diana Solana-Sodeinde, US FDA, presented an update on FDA's Inactive Ingredient Database (IID). GDUFA III has confirmed commitment (Fiscal years 2023-2027) to continue enhancements to the IID to enable users to perform electronic queries to reference accurate maximum daily intake and maximum daily exposure (MDE) information for each route of administration for which data are available. Currently 42% of the records in the IID include MDE information. FDA will update the IID on an ongoing basis and will post a quarterly notice of updates made. Also, OGD is dedicated to completing IID updates for priority excipients such as, but not limited to, polysorbate, MCC, HPC, PEO, silicon dioxide, etc. A special case has been made for Red dye No 3 (Erythrosine). A Federal Registration Notice was posted on Jan 15, 2025. Red No3, erythrosine, is no longer on the IID because the FDA revised the CFR color additive regulations to remove it. Drug manufacturers have until Jan 18, 2028, to remove this color additive from products.

## CONCLUSION

It is hoped that this snapshot of Excipient World 2025 generates your interest and enthusiasm to participate in the meeting next year, as a participant or as a presenter. Obviously, this report doesn't do the meeting complete justice as it only highlights a certain amount of the content covered. There were other talks by various companies, several additional contributions by the USP and the informative scientific poster session. All contributions fed into the theme of a "time for change" by building knowledge relevant to current trends, highlighting scientific advances, and visioning future regulatory landscapes. Sea changes can have positive or negative consequences and to achieve the best outcomes we must work together to promote the importance of excipients. The Excipient World Conference represents a valuable mechanism for coming together for the benefit of our industry by fostering exchange of contemporary and pre-emptive scientific, regulatory, and business information pertinent to excipients and their evolving roles in pharmaceutical, biotech and veterinary product development.

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