



TFOS DEWS II Introduction



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The initial focus on dry eye disease (DED) began with the publication of the report of the National Eye Institute/Industry Workshop on Clinical Trials in Dry Eye in 1995. It was the first formal attempt to define and classify DED, in addition to reviewing its management, treatment, and the design of clinical trials. This was

followed in 2007 with the Tear Film and Ocular Surface Society (TFOS) publication of the Report of the TFOS International Dry Eye Workshop that has become widely known as TFOS DEWS (Ocul Surf 2007; 5(2): 65–204). The workshop consisted of 58 members from 11 countries, had seven subcommittees and was 140 pages in length. Now, 10 years later, progress continues with the publication of this 2017 Report of the TFOS International Dry Eye Workshop II (TFOS DEWS II). This workshop, a two-year effort for 12 Subcommittees made up of 150 experts from 23 countries, has led to the creation and publication of this substantial report.

Why such a lengthy report? Since publication of the first TFOS DEWS report, the number of publications relating to dry eye has almost doubled [Fig. 1].

TFOS DEWS II Steering Committee

The 25-member TFOS DEWS II Steering Committee [Table 1] was responsible for developing the specific aims and mission, along with the strategy, tactics, structure, methods of communication, timeline, milestones and conflict of interest policy. The Steering Committee agreed upon Workshop topics, selected Subcommittee Chairs and members, proposed guidelines for determining the acceptable levels of evidence and methods of documentation to support such evidence, and considered the most appropriate journal to which publication would be directed.

Objectives

The TFOS DEWS II Steering Committee committed to an evidence-based approach and a process of open communication, dialogue and transparency, in order to achieve a consensus concerning multiple aspects of DED. The committee formulated the workshop objectives, which were to:

1. Update the definition, classification and diagnosis of DED;
2. Critically assess the etiology, mechanism, distribution and impact of this disorder; and
3. Address its management and therapy

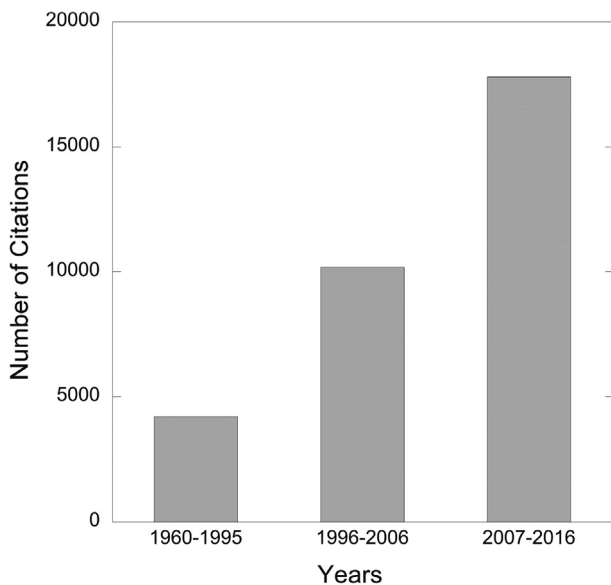


Fig. 1. The number of Dry Eye citations prior to the NEI/Industry Report (1960–1995); new citations between the NEI/Industry Report to the TFOS DEWS Report (1998–2007); and new citations between the TFOS DEWS and TFOS DEWS II Reports.

Table 1
Steering committee members.

Nelson, J Daniel (Chair; USA)
Craig, Jennifer P (Vice Chair; New Zealand)
Sullivan, David A (Organizer; USA)
Akpek, Esen (USA)
Azar, Dimitri (USA)
Belmonte, Carlos (Spain)
Bron, Anthony (UK)
Clayton, Janine (USA)
Dogru Murat (Japan)
Dua, Harinder (UK)
Foulks, Gary (USA)
Gomes, José (Brazil)
Hammit, Katherine (USA)
Holopainen, Juha (Finland)
Jones, Lyndon (Canada)
Joo, Choun-Ki (South Korea)
Liu, Zuguo (China)
Nichols, Jason (USA)
Nichols, Kelly (USA)
Novack, Gary (USA)
Sangwan, Virender (India)
Stapleton, Fiona (Australia)
Tsubota, Kazuo (Japan)
Willcox, Mark (Australia)
Wolffsohn James (UK)
Consultant
Tomlinson, Alan (UK)

TFOS DEWS II subcommittees

In order to fulfill these objectives, the Steering Committee, meeting in San Francisco, CA, USA in March 2015, created 12 Subcommittees:

Definition & Classification (10)*	Iatrogenic Dry Eye (13)
Sex, Gender & Hormones (11)	Diagnostic Methodology (16)
Epidemiology (12)	Management & Therapy (14)
Tear Film (13)	Clinical Trial Design (10)
Pain & Sensation (14)	Public Awareness & Education (14)
Pathophysiology (13)	Industry Liaison (16)

*The numbers within the parentheses represent the final number of Subcommittee members.

The Public Awareness and Education Subcommittee was created to take responsibility for helping to make recommendations for communicating the conclusions and recommendations of all other Subcommittees to the lay person. To aid in this effort, this group sent representatives to each of the other Subcommittee meetings. The Industry Liaison Subcommittee was created to provide proactive and reactive comments about the goals of, and draft reports from, all other Subcommittees. Members of this Subcommittee sought constructive input from appropriate individuals in their companies about the TFOS DEWS II goals and draft reports. Members then forwarded their critiques for distribution to specific Subcommittees for their consideration. Subcommittees then carefully considered whether or not to include liaison recommendations in their reports. In this way the TFOS DEWS II process was able to benefit from the collective experience and knowledge of these sponsoring companies, which, in turn, helped in promoting a consensus in Workshop conclusions and recommendations.

The TFOS DEWS II Chair, Vice-Chair and Organizer developed the qualifications for participation and responsibilities of all Workshop members. The Steering Committee appointed Chairs for

each of the 12 individual Subcommittees. In addition, 139 experts in their respective fields were chosen, based on their global representation and multidisciplinary clinical, research and patient perspectives, from a much larger pool of individuals who had been nominated and/or expressed written interest in participating in TFOS DEWS II. Four of these experts were assigned to serve on two Subcommittees, and two other individuals were invited as Consultants. After this selection process, 4 individuals withdrew because of other commitments and 15 Industry Liaison members were invited, which yielded the total of 150 TFOS DEWS II participants [Table 2].

Workshop process & progress

Individual Subcommittee meetings were subsequently held around the world (Barcelona, New York, Paris, Las Vegas, London, and Washington, DC) between June and November 2015. Draft outlines of each Subcommittee report were developed and submitted after these meetings and reviewed by the TFOS DEWS II membership to identify overlap or gaps. Subcommittee Chairs met in London in early November 2015 to review progress to date and to refine and approve the draft outlines.

Between November 2015 and April 2016, Subcommittees developed draft reports and circulated them to the entire TFOS DEWS II membership for comment. All available members of TFOS DEWS II then met at a post-ARVO meeting in May 2016 in Seattle, WA, USA. Each Subcommittee Chair delivered a summary presentation of their Subcommittee's draft report. The TFOS DEWS II membership had opportunity to discuss, ask critical questions, and give comments and make suggestions. The Subcommittees were then charged to refine their draft reports based on written and oral comments and develop their final reports by October 2016. Updates of these reports were again presented in summary form at the TFOS 2016 Conference (September; Montpellier, France), prior to the full reports being circulated to the TFOS DEWS II membership for final comment. Member critiques were addressed in the final Subcommittee reports. Subcommittee reports were then turned over to the appointed Harmonization Committee (Table 3) for final editorial and content review in late 2016. The Harmonization Committee met in Sydney, Australia in early January 2017 to finalize the reports and prepare them for submission for publication.

A major difficulty in the process was dealing with the definition of DED. It became obvious during the almost 2-year process of literature review, discussion and writing of reports, that the definition of DED needed to be developed after all the reports had been written (and read) and not before, as it was critical that the definition was evidence-based. A group of 8 individuals¹ met in early December 2016 in St. Paul, MN, USA to further refine the Definition & Classification Subcommittee's definition of DED in the context of the other completed reports.

Subcommittee issues, controversies, and advancements

Definition & classification

There has been much controversy over the past 20 years regarding the appropriate definition for dry eye. The NEI/Industry definition [1] stated:

Dry eye is a disorder of the tear film due to tear deficiency or excessive tear evaporation, which causes damage to the

interpalpebral ocular surface and is associated with symptoms of discomfort.

Table 2
Subcommittee members.

Definition and Classification

Craig, Jennifer P (Co-Chair; New Zealand)
Nichols, Kelly K (Co-Chair; USA)
Akpek, Esen (USA)
Caffery, Barbara (Canada)
Dua, Harminder (UK)
Joo, Choun-Ki (Korea)
Liu, Zuguo (China)
Nelson, J Daniel (USA)
Nichols, Jason (USA)
Tsubota, Kazuo (Japan)

Sex, Gender, and Hormones

Sullivan, David A (Chair; USA)
Aragona, Pasquale (Italy)
Clayton, Janine (USA)
Ding, Juan (USA)
Golebiowski, Blanka (Australia)
Hampel, Ulrike (Germany)
McDermott, Alison (USA)
Rocha, Eduardo (Brazil)
Schaumberg, Debra (USA)
Srinivasan, Sruthi (Canada)
Versura, Piera (Italy)

Epidemiology

Stapleton, Fiona (Chair; Australia)
Alves, Monica (Brazil)
Bunya, Vatinnee (USA)
Jalbert, Isabelle (Australia)
Lekhanont, Kaevalin (Thailand)
Malet, Florence (France)
Na, Kyung-Sun (Korea)
Schaumberg, Debra (USA)
Uchino, Miki (Japan)
Vehof, Jelle (The Netherlands)
Viso, Eloy (Spain)
Vitale, Susan (USA)

Tear Film

Willcox, Mark DP (Chair; Australia)
Argüeso, Pablo (USA)
Georgiev, Georgi (Bulgaria)
Holopainen, Juha (Finland)
Laurie, Gordon (USA)
Millar, Thomas (Australia)
Papas, Eric (Australia)
Rolland-Thompson, Jannick (USA)
Schmidt, Tannin (Canada)
Stahl, Ulrike (Canada)
Suárez, Tatiana (Spain)
Subbaraman, Lakshman (Canada)
Uçakhan, Ömür (Turkey)

Pain and Sensation

Belmonte, Carlos (Co-Chair; Spain)
Nichols, Jason (Co-Chair; USA)
Begley, Carolyn (USA)
Bereiter, David (USA)
Brock, James (Australia)
Cox, Stephanie (USA)
Dartt, Darlene (USA)
Galor, Anat (USA)
Hamrah, Pedram (USA)
Ivanusic, Jason (Australia)
Jacobs, Deborah (USA)
McNamara, Nancy (USA)
Rosenblatt, Mark (USA)
Stapleton, Fiona (Australia)

Pathophysiology

Bron, Anthony J (Chair; UK)
Chauhan, Sunil K (Co-Chair; USA)
de Paiva, Cintia S (Co-Chair; USA)
Bonini, Stefano (Italy)
Gabison, Eric (France)

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Table 2 (continued)

Jain, Sandeep (USA)
Knop, Erich (Germany)
Markoulli, Maria (Australia)
Ogawa, Yoko (Japan)
Perez, Victor (USA)
Uchino, Yuichi (Japan)
Yokoi, Norihiko (Japan)
Zoukhri, Driss (USA)
Iatrogenic Dry Eye
Gomes, José AP (Chair; Brazil)
Azar, Dimitri (Co-Chair; USA)
Baudouin, Christophe (France)
Efron, Nathan (Australia)
Hirayama, Masatoshi (Japan)
Horwath-Winter, Jutta (Austria)
Kim, Terry (USA)
Mehta, Jodhbir Singh (Singapore)
Messmer, Elisabeth (Germany)
Pepose, Jay (USA)
Sangwan, Virender (India)
Weiner, Alan (USA)
Wilson, Steven (USA)
Diagnostic Methodology
Wolffsohn, James S (Chair; UK)
Arita, Reiko (Japan)
Chalmers, Robin (USA)
Djalilian, Ali (USA)
Dogru, Murat (Japan)
Dumbleton, Kathryn (UK)
Gupta Preeya (USA)
Jones, Lyndon (Canada)
Karpecki, Paul (USA)
Lazreg, Sihem (Algeria)
Pult, Heiko (Germany)
Sullivan, Benjamin D (USA)
Tomlinson, Alan (UK)
Tong, Louis (Singapore)
Yoon, Kyung Chul (Korea)
Villani, Edoardo (Italy)
Management and Therapy
Jones, Lyndon (Chair; Canada)
Benitez Del Castillo Sanchez, Jose (Spain)
Dana, Reza (USA)
Deng, Sophie (USA)
Dong, Pham Ngoc (Viet Nam)
Downie, Laura (Australia)
Geerling, Gerd (Germany)
Hida, Richard Yudi (Brazil)
Korb, Donald (USA)
Liu, Yang (USA/China)
Seo, Kyoung Yul (South Korea)
Tauber, Joseph (USA)
Wakamatsu, Tais (Brazil)
Xu, Jianjiang (China)
Clinical Trial Design
Novack, Gary D (Chair; USA)
Asbell, Penny (USA)
Barabino, Stefano (Italy)
Bergamini, Michael (USA)
Ciolino, Joseph (USA)
Foulks, Gary (USA)
Goldstein, Michael (USA)
Lemp, Michael (USA)
Schrader, Stefan (Germany)
Woods, Craig (Australia)
Public Awareness and Education
Hammit, Katherine M (Chair, USA)
Bitton, Etty (Canada)
Cohen, Stephen (USA)
Epstein, Arthur (USA)
Gupta Preeya (USA)
Marini, Cecilia (Argentina)
O'Dell, Leslie (USA)
Parsloe, Colin (UK)
Petris, Rebecca (USA)
Perry, Christina (USA)
Shen, Joanne (USA)

Table 2 (continued)

Starr, Christopher (USA)
Suh, Leejee H (USA)
Ubels, John (USA)
Consultant
Sullivan, Amy Gallant (USA)
Industry Liaison
Sullivan, David A (Chair; USA)
Ackerman, Michael (Oculeve)
Couderc, Chantal (Horus)
Dempsey, Robert (Shire)
Houtman, Diane (Akorn)
Mark C Jasek (Sun Pharma)
Keir, Nancy (CooperVision)
Kern, Jami R (Alcon)
Koffler, Dawn (Allergan)
Mantelli, Flavio (Dompé)
Mazzone, Maria Grazia (SIFI)
Myering, Robert J (Bausch+Lomb)
Purslow, Christine (Laboratoires Théa)
Speed, Julie (TearLab)
Truitt, Edward R, III (Lubris)
Wilson, Tawnya (Johnson & Johnson Vision Care)

At this stage dry eye was termed a “disorder” of the tear film with signs and symptoms attributed to tear deficiency or excessive evaporation. However, it lacked description of any specific patho-physiologic basis.

The TFOS DEWS definition [2] updated the definition to:

Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.

This was the first time that dry eye had been identified as a disease, with many underlying causes, that was deemed to result in symptoms and signs, in association with tear film hyperosmolarity and ocular surface inflammation. The inclusion of these associations was a stumbling block for many, who interpreted them as primarily diagnostic criteria.

The newly developed TFOS DEWS II definition states:

Dry eye is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neuro-sensory abnormalities play etiologic roles.

Inclusion of the phrase “loss of homeostasis” is novel, and this definition clarified, based on recent peer-reviewed evidence, that tear film hyperosmolarity and ocular surface inflammation have causal etiologic roles, along with the addition of neurosensory abnormalities (contributing to the common mismatch between signs and symptoms).

Table 3

Harmonization committee members.

Nelson, J Daniel (Chair; USA)
Craig, Jennifer P (Vice Chair; New Zealand)
Sullivan, David A (Organizer; USA)
Jones, Lyndon (Canada)
Stapleton, Fiona J (Australia)
Willcox, Mark DP (Australia)
Wolffsohn, James S (UK)

Each preceding definition has brought us forward in our understanding of DED and has stimulated research and investigation into the underlying causes and treatments for DED as, it is anticipated, will this updated definition.

Sex, gender & hormones

That DED occurs more frequently in women than men suggests there are sex-related differences underlying its etiology. There is a difference between sex and gender. Sex refers to the classification of living things according to their reproductive organs and functions assigned by chromosomal complement, i.e., male and female. Gender refers to a person's self-representation as a man or woman, or how social institutions respond to that person based upon the individual's gender presentation. While sex, gender, and hormones play a major role in the regulation of the ocular surface and adnexal tissues, and in the difference in DED prevalence between men and women, further research is needed to clarify the precise nature, extent, and mechanisms of these sex, gender, and endocrine effects on the eye in health and disease. A deeper understanding of these issues may result in improved, more tailored and appropriate options for the treatment of DED.

Epidemiology

The epidemiology of DED continues to be a challenge due to the lack of a standardized worldwide definition. This has resulted in epidemiologic studies using different diagnostic criteria based on symptoms and signs and self-reported diagnoses. Although new information on the prevalence of DED has been published since the initial TFOS DEWS report, there is only one population-based study on the prevalence of DED south of the equator, with much of the attention being focused on Asia and Europe. The prevalence of DED, with and without symptoms, ranges from 5 to 50%. Prevalence of DED based on signs only is even more variable, reaching up to 75% in some populations. The challenge is that the criteria for positive signs have varied between studies, which may reflect secondary outcomes, or be attributed to aging changes.

To date, very few studies have been conducted in younger populations and this information may be very valuable as the data published so far suggests a lower prevalence of DED in younger subjects. What is it about these individuals that is different? Is it tear film composition, tear thickness, lid differences in tightness or shape, corneal or conjunctival sensitivity? Asian ethnicity appears to be a risk factor, but the reason for this is, as yet, unclear. Higher rates of DED in women compared to men only become significant with increasing age. The most severe economic impact of DED likely results from indirect costs related to decreased work productivity. Future needs include a detailed evaluation of the prevalence of DED of varying severity, prevalence in youth, incidence studies in various populations, and the impact of the use of current technologies, such as mobile devices. The effects of climate, environmental and socioeconomic factors deserve further study. Finally, the natural history of DED in treated and untreated individuals remains an important area for future research.

Tear film

DED implies major changes to the tear film structure and function, which are associated with this disease. Historically, the tear film has been viewed as a 3-layer "sandwich" composed of distinct lipid, aqueous and mucin layers. Evidence continues to support the more contemporary two-phase model of the tear film, with a lipid layer overlying a mucoaqueous phase. While it may be that the whole tear film (lipids, mucins, proteins and salts) prevents

tear film evaporation and collapse, additional studies are needed to confirm or deny this concept. The lipid layer contains polar and non-polar lipids. The mucoaqueous layer contains at least four major mucins and over 1500 different proteins and peptides and overlies the carbohydrate-rich glycocalyx of the apical epithelium. While tear proteins are reported to change in DED, no definitive set of proteins or changes in protein levels have been validated to aid in diagnosis. There is a need to further characterize the biochemistry of the tear film to identify new markers that can be used to diagnose, and perhaps predict and treat, DED. There is also a need for ways to dynamically measure tear film osmolarity and markers of inflammation over the whole ocular surface.

Pain & sensation

Nociceptive pain occurs in response to actual or threatened damage to tissues, while neuropathic pain occurs due to a lesion within the somatosensory nervous system. Sensory nerves comprise polymodal nociceptor neurons, pure mechano-nociceptor neurons, and cold thermoreceptor neurons. Polymodal nociceptors respond to chemical, mechanical, and thermal stimuli and are sensitized by inflammatory mediators. Mechano-receptors respond to mechanical forces. Cold thermoreceptors continuously discharge nerve impulses at the normal ocular surface temperature, responding to warming or cooling and to osmolarity increases, likely contributing to reflex control of basal tear production and blinking. Studies to date suggest potential merit in exploring treatment strategies involving cold receptors to manage DED symptoms.

The main lacrimal gland is regulated by autonomic sympathetic and parasympathetic innervations, which, in turn, are regulated by reflex influences from sensory neurons supplying the ocular surface. Little is known about the neuronal control of the accessory lacrimal glands. Similarly, only a single study to date has shown a role for sensory or autonomic nerves or their neurotransmitters in meibomian gland regulation. Although activation of sensory neurons in the rat cornea results in goblet cell secretion, the efferent nerve type(s) involved in this reflex remain to be established. Inflammation causes sensitization of polymodal and mechano-receptors and depresses cold thermoreceptor activity. However, the most prominent nerve disturbance is with the cold thermoreceptors, suggesting that dryness-induced nerve damage dominates over inflammation, again emphasizing a need to focus on possible treatment strategies involving cold thermoreceptors.

Pathophysiology

Meibomian gland dysfunction (MGD) and Sjögren and non-Sjögren lacrimal disease remain leading causes of evaporative and aqueous-deficient DED, respectively, and many hybrid forms of DED exist. The core mechanism of DED is tear hyperosmolarity, which is the hallmark of the disease. It damages the ocular surface both directly and by initiating inflammation. These sequelae lead to a cycle of events termed the Vicious Circle, that explains how ocular surface damage is initiated and perpetuated in DED. Tear hyperosmolarity, as well as inflammatory mediators, may induce DED symptoms and cause damage to epithelial cells, surface microvilli, barrier function, the glycocalyx, and goblet cells. Epithelial cell damage, lipid layer and blinking abnormalities, defective glycocalyx, loss of gel mucin and reduction in tear volume may result in loss of lubrication between the globe and eyelids, resulting in increased friction and also symptoms. The role of increased friction in DED and its subsequent sequelae deserves further investigation.

Inflammation of the ocular surface can cause inhibition of lacrimal secretion and loss of epithelial barrier function at the ocular surface. Tear film breakup, leading to localized

hyperosmolarity, can result in ocular surface damage either directly or through the cascade of inflammation that it initiates. Improved understanding of the role of subclinical inflammation in the early stages of DED also warrants further study.

Iatrogenic dry eye

Topical and systemic medications, contact lenses, ophthalmic surgeries, and non-surgical procedures can cause DED. Preservatives such as benzalkonium chloride in ophthalmic formulations can exacerbate DED through toxic and pro-inflammatory effects. Systemic medications can result in decreased tear production, altered sensory input, and reflex tear secretion. Contact lenses and their associated care solutions can induce DED. Refractive and corneal surgeries can cause or aggravate DED due to the transection of corneal nerves or through the use of post-operative topical medications. Cosmetic and functional eyelid surgeries, botulinum toxin injections, and even cataract surgery, along with their post-procedure topical medications, can lead to DED. Future recommendations for research include conducting further epidemiologic studies to better define risk factors, creating less toxic medications and preservatives, devising less invasive ophthalmic procedures, and developing strategies for the detection of early DED prior to surgical interventions.

Diagnostic methodology

The sensitivity and specificity of tests for the diagnosis of DED are highly dependent on the inclusion criteria for DED, the severity of the disease group, and the population studied. The research evidence suggests that the best clinical approach involves the use of triaging questions and risk factor analysis as part of a traditional patient history, leading to a detailed anterior eye examination and differential diagnosis based on the answers. If DED is suspected, a positive result to a screening questionnaire such as the 5-item Dry Eye Questionnaire (DEQ-5) or the Ocular Surface Disease Index (OSDI) should trigger further evaluation, with tear break-up time (non-invasive methods preferred), tear film osmolarity determination, and ocular surface staining (that includes the cornea, conjunctiva and lid margin) with fluorescein and lissamine green. Identification of a disruption in tear film homeostasis with these tests, allows a diagnosis of dry eye to be made. This standardized approach will facilitate improved epidemiological DED research and therapeutic regulatory approvals in the future. Other tests, such as meibography, lipid layer interferometry, evaporation and tear volume measurements can help clarify where the individual with DED falls on the evaporative and aqueous deficient DED subtype classification spectrum and promote the selection of appropriate therapeutic interventions. New approaches and better-validated instrumentation and techniques are needed to more critically assess DED and to link underlying causes in an individual to the most suitable therapies to manage their DED.

Management & therapy

Restoration of tear film homeostasis is the ultimate goal in the management of DED, and this involves breaking the Vicious Circle of the disease. Determining whether the major cause(s) of an individual's DED pertains predominantly to aqueous tear deficiency or to evaporative causes, or both, is critical in helping select the most appropriate management strategy. Our failure in resolving patient symptoms and signs of DED may relate more to a lack of success in determining and targeting the underlying nature or cause of a patient's DED than a failure of the treatment itself. Management of DED is often complex. The challenge remains to

develop management and treatment strategies that are not overly complicated for our patients. Although staged management and treatment recommendations are presented, the heterogeneity of the DED patient population mandates that practitioners manage and treat patients based on individual profiles, characteristics and responses. Additional topical therapies that are effective and inexpensive are needed.

Clinical trials

Clinical trial conduct should be consistent with Good Clinical Practice, including the use of Good Manufacturing Practice quality clinical trial materials. Design, treatments, and sample size need to align with the investigational treatment, the objectives of the study, and the phase of development. For pivotal studies, there should be *a priori* selection of the outcome measure, and an appropriate sample size.

Dedication

This workshop report is dedicated to the late Professor Juha Holopainen (Helsinki Eye Lab and Department of Ophthalmology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland), who served on the Steering Committee and Tear Film Subcommittee, in recognition of his outstanding scientific contributions to the field of the ocular surface and tear film.

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J. D. Nelson, Chair: TearSolutions (I, C, R), Santen (F, C), Editor in Chief, Ocular Surface (F).

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D. A. Sullivan, Organizer: Allergan, Cempra, GlaxoSmithKline, Novagali/Santen, TearLab, (F); Singularis (I); M.G. Therapeutics (C); Dompé, Fovea, Laboratoire Théa, Lμβris Sanofi/Novartis, (R).

E. Akpek: Allergan (F); Biogen, Seattle Genetics, GSK, Nicox (C).

D. Azar: Novartis/Alcon, Google, Chicago Medical Society (F); Novartis, Google, (I); University of Illinois (E); Alcon/Google (C); Novartis/Alcon/Google (R).

C. Belmonte: Avizorex Pharma, (F) (I) (C) (P) (R); Coopervision (F).

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M. Dogru: Otsuka Pharmaceuticals (F), Santen (F).

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