Creating vision
beyond what we see

Ora CAE

The Ora Controlled Adverse Environment (CAE®) minimizes influential factors by standardizing temperature, humidity, airflow, lighting, and visual tasking. By creating a constant and reproducible challenge, CAE® offers industry leading precision with fewer patients, fewer sites, and less time.

- The Ora CAE® technology provides controlled environmental stress that creates a consistent and replicable patient response. Use of the CAE® turns down the noise in our sponsor's clinical dataset to improve the power of their novel therapeutic study.
- Ora Controlled Adverse Environment (CAE®) is accepted by the FDA for Phase 2 and 3 studies as a primary endpoint in the US.
- Ora CAE® model can be individually tailored to all therapeutic modalities for the treatment of Dry Eye Disease (DED) such as: anti-inflammatories, wound healing peptides, secretagogues, hormonal, artificial tears, rewetting solutions, and contact lenses.

Above: *Mobile CAE Units*

The acceleration of DED research has intensified over the past several decades. As a result, the knowledge surrounding the pathophysiology of DED has increased as well. The innovation evolution of the dry eye pipeline is never-ending, from investigational therapies and devices to engineering clinical models, study designs, and technologies. Thus, Ora's in house R&D team is on a mission for constant improvement of endpoints and approaches to ensure we:

1. **Accurately measure product efficacy.**
2. **Fully understand therapeutic impact.**
3. **Streamline clinical designs and sample requirements.**

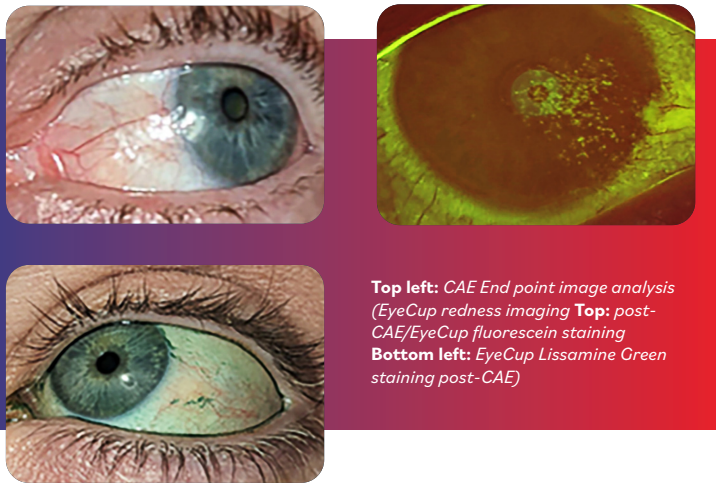
Ora's CAE® Controlled Adverse Environment is a DED model that exacerbates signs and symptoms of the disease in a controlled environment. When study patients enter a controlled chamber and are exposed to Ora's CAE® Dry Eye Challenge in terms of relative humidity, temperature, airflow, lighting conditions, and visual tasking, the ocular surface is stressed to react[1]. This controlled environmental stress creates a consistent patient response that is reproducible over time. As a result, data derived from the CAE® model offers greater precision in predicting the efficacy of a drug – with fewer patients, fewer sites, and less time.

The Ora CAE® Dry Eye Challenge creates the ideal paradigm for identifying:

1. An enriched population of dry eye patients with modifiable signs and symptoms.
2. Endpoints for intervention that show relevant change.

Our vast and experienced team at Ora will provide a menu of trial designs within the context of CAE®. We work with YOU to determine the right approach for your product. Furthermore, our Mobile Dry Eye Units enable multi-center dry eye trials while still reducing clinical variables among sites. With Ora, you can bring your clinical trial to your patient. The Ora CAE® Model can be:

- Tailored to the mechanism of action (MOA) of the therapeutic to be tested.
- Used as an enrichment tool to identify and enroll the appropriate patient population for each clinical study design.
- Relied on to provide endpoints that demonstrate change with therapeutic intervention.
- Used at multiple sites across the globe.



Top left: *CAE End point image analysis (EyeCup redness imaging* **Top:** *post-CAE/EyeCup fluorescein staining* **Bottom left:** *EyeCup Lissamine Green staining post-CAE)*

CAE® Case Study Example: SARcode Bioscience (a start-up company) and Xiidra® approval. Involved a program conducted in the US where patients were suffering from signs and symptoms of DED. Ora CAE® was used as a screening tool along with the Ora Calibra® Scales to identify a primary symptom sign (inferior corneal staining) in enrolled patients. The inferior corneal staining was highly reproducible, and the success of the Phases 2 and 3 study contributed to the eventual product approval. With the help of CAE®, SARcode was able to license the technology to a large pharmaceutical company. Most importantly, it led to the first DED product to be approved for the treatment of both the signs and symptoms of the disease.

Above: *New capabilities of CAE 2.0 (real-time patient feedback and A.I. measurement of fissure height).*

The evolution of the Ora CAE® Technology

Despite the undeniable success and reproducibility of the tried-and-true Ora CAE® technology, the Ora R&D team has been working hard to improve on the already impressive CAE® system.

Future Capabilities of CAE® 2.0:

1. Duration of the test time has been cut in half from 90 minutes to 45 minutes.
2. Utilization of a camera enabled with an artificial intelligence-based algorithm to track the test subject's gaze and blink rate throughout the test.
3. Titratability of the CAE 2.0 airflow that is controlled by subject's fissure height.

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References

1. Ousler GW 3rd, Rimmer D, Smith LM, Abelson MB. Use of the Controlled Adverse Environment (CAE) in Clinical Research: A Review. Ophthalmol Ther. 2017;6(2):263-276.

Ora

Ora is a global full-service ophthalmic drug and device development firm with vast capabilities through all steps of clinical research, including preclinical, clinical, CMC & regulatory, and patient and site evaluations. Through Ora's 40+ years of experience, the company has assisted in bringing more than 80 products to market. Ora's team of experts utilizes global regulatory strategies, integrated research operations, and extensive site and patient engagement to accelerate product development in anterior and posterior segment, as well as ophthalmic devices.