White Paper

Alcon

TOTAL30® CONTACT LENSES WITH WATER GRADIENT AND CELLIGENT® TECHNOLOGIES

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KEY TAKEAWAY POINTS

- Limited advancements in contact lens materials and properties have occurred in the monthly replacement category in the past decade
- TOTAL30® contact lenses are the first and only monthly replacement lenses that include Water Gradient Technology
- TOTAL30® contact lenses feature Celligent® Technology, which has biomimetic properties that allow the lens to mimic the corneal surface
- The innovative surface chemistry provides an extremely soft and lubricious lens surface and helps to resist bacterial and lipid deposit adhesion

MONTHLY CONTACT LENS ADVANCEMENTS

While contact lens users vary in their replacement schedule preference, the reusable category is the most prevalent at approximately 60% of the contact lens market in the U.S.[1] Over time, there have been many improvements to contact lens materials and properties, although few of these advancements have occurred in the monthly replacement category. New technologies are needed for those patients who prefer to wear monthly replacement lenses.

TOTAL30® CONTACT LENSES WITH WATER GRADIENT AND CELLIGENT® TECHNOLOGY

Alcon introduces TOTAL30® contact lenses, the first and only monthly replacement lenses that include Water Gradient Technology, the breakthrough technology found in DAILIES TOTAL1® lenses. TOTAL30® (lehfilcon A) lenses have a 55% water content at the core that gradually increases to nearly 100% water at the outer surface (Figure 1).[2] The silicone hydrogel core allows for high oxygen permeability (Dk/t: 154 @ -3D) and a core modulus of 0.6 MPa for easy handling (Figure 2).[3] The permanent water surface consists of bound hydrogel polymers providing high lens surface wettability and making the surface ultrasoft to support on-eye comfort.[4] A defining feature of TOTAL30® contact lenses is the biomimetic Celligent® Technology, which allows the lens to mimic the structure of the ocular surface.[5]

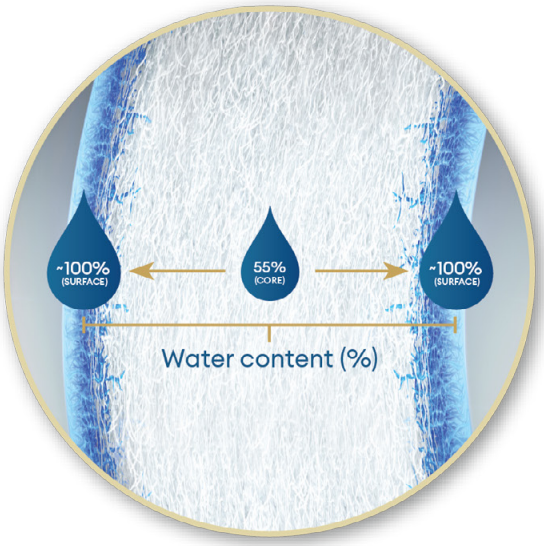


Figure 1: TOTAL30® Contact Lens Core and Surface Water Content

MATERIAL lehfilcon A	**CENTER THICKNESS (@-3.00D, mm)** 0.08	**CORE MODULUS (MPa)** 0.6
DIAMETER (mm) 14.2	**HANDLING TINT** VISITINT®	**SURFACE MODULUS (MPa)** 0.046
Dk/t 154 @ -3.00D	**SURFACE WATER CONTENT** -100%	**PACKAGING** 6-ct. box and 1-ct. trial pack
BASE CURVE (mm) 8.4	**CORE WATER CONTENT** 55%	**LIGHT PROPERTIES** Class I UV abosrption* and HEVL filtration**
POWER RANGE +8.00D to +6.50D (0.50D steps); +6.00D to +0.25D (0.25D steps); -0.25D to -8.00D (0.25D steps); -8.50D to -12.00D (0.5D steps)		**WEARING SCHEDULE** Daily wear only

Figure 2: TOTAL30® Contact Lens Parameters

WHAT IS CELLIGENT® TECHNOLOGY?

Celligent® Technology was inspired by the biology of the ocular surface in order to create a new level of biomimicking properties in a monthly contact lens. Celligent® Technology in Total30® supports a monthly replacement schedule and requires use of lens care solutions for cleaning, disinfecting and storage. Alcon took the Water Gradient Technology, first introduced in DAILIES TOTAL1®, and adapted it with Celligent® Technology to form the Water Gradient surface. The innovative Celligent® Technology also allows for lipid and bacterial adhesion resistance, which is important for a monthly replacement contact lens.[6,7,8]

The surface of TOTAL30® features a polymer structure very different than its core. The lens surface was created to have a similar structure to the glycocalyx on the cornea. The surface polymers (2-methacryloyloxyethyl phosphorylcholine, MPC) create nanofiber structure on the TOTAL30® lens surface that is like the nanofiber structure of the glycocalyx on the corneal surface (Figure 3).[5] Therefore, the structure of the glycocalyx is mimicked by the Celligent® Technology giving TOTAL30® contact lenses its biomimetic properties. MPC has demonstrated biocompatible properties and benefits within the body. These polymers have been used in several other applications (i.e. grafts, implants) and have shown to help reduce protein, bacteria and cell adhesion.[8,9] It is these characteristics that were the basis behind the development of Celligent® Technology on TOTAL30® contact lenses. The glycocalyx of the cornea is what also helps to hold the tear film onto the ocular surface, reduces frictional forces with the eyelid during each blink and serves as a barrier to microbes. Similarly, the polymer nanofibers on the TOTAL30® lens surface draw water into the lens surface to create and maintain the water gradient, giving it lubricity and softness and also helps to protect against lipid and bacteria deposition.[2,6,7,8]

The surface of the TOTAL30® contact lenses have both positive and negative charges close together creating a net neutral charge.[8,10] This is important since lens care biocides are charged molecules that can uptake and release from contact lens surfaces based on the interactions with the net lens material surface charge. This feature of TOTAL30® contact lenses allows for minimal preservative uptake when stored in lens care solutions and supports its resistance to surface deposits and bacteria. Further, the net neutral charge of the MPC polymer structure is able to attract smaller molecules like water to the water gradient layer and concurrently help resist adhesion of larger bacteria and lipids.[6,7,8,10] The nanofiber structure of Celligent® Technology in TOTAL30® contact lenses is permanent and remains intact for a full month of daily lens wear with cleaning, disinfecting and storing (Figure 4).[5]

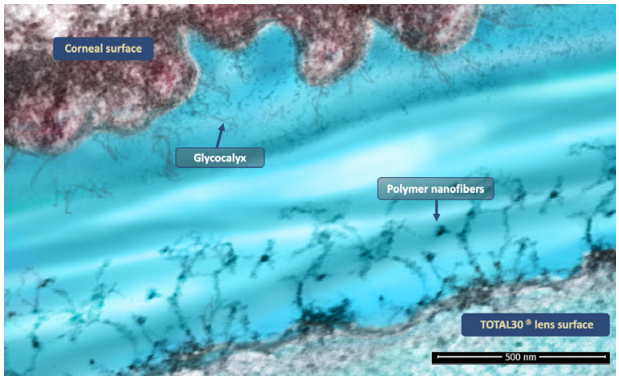


Figure 3: Similarity of the TOTAL30® Polymer Nanofiber Contact Lens Surface to the Corneal Glycocalyx (scanning transmission electron microscope (STEM) imaging)

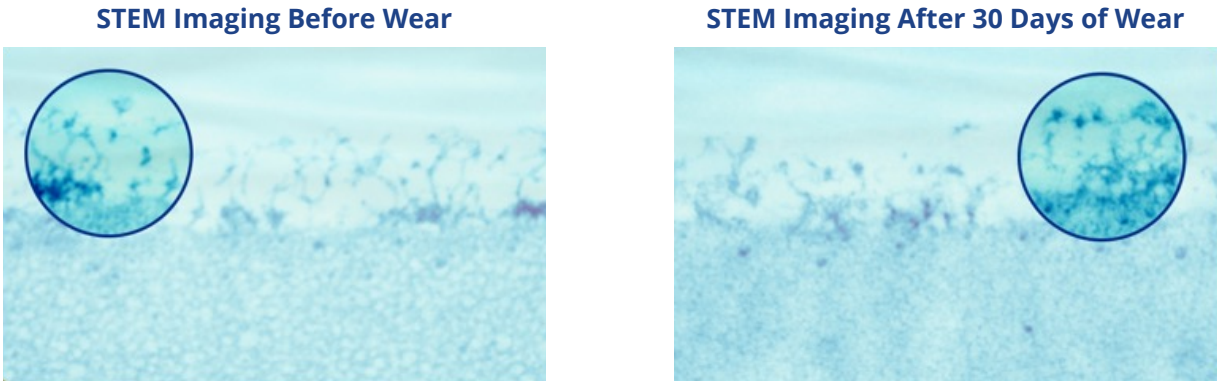


Figure 4: Scanning transmission electron microscope (STEM) imaging of the TOTAL30® lens surface before wear and after 30 days of daily wear with cleaning/disinfecting/storage. A) A new unworn TOTAL30® lens surface showing polymer nano-fiber protrusions (similar to that of the glycocalyx); B) ex-vivo TOTAL30® lens surface after 30 days of wear and care demonstrating that the nano-fiber surface is still fully intact.[5]

Additional features offered by TOTAL30® contact lenses include UV and HEVL filtering. TOTAL30® contact lenses include Class I UV absorption for protection against UVA and UVB rays, filtering more than 90% of UVA and 99% of UVB rays.[11*] TOTAL30® contact lenses also filter out approximately 34% of high-energy visible light (HEVL) rays entering the eye (between 380-450nm) (Figure 5).[11**] TOTAL30® is the first contact lens to offer HEVL filtering capability that is constantly in effect while wearing the lenses regardless of the lighting conditions.

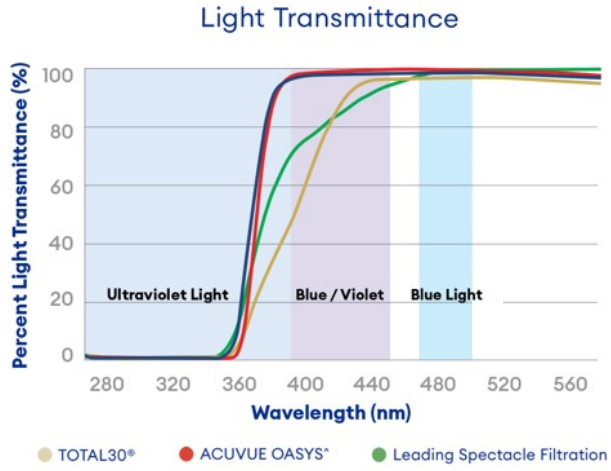


Figure 5: Light transmittance properties of TOTAL30®, ACUVUE OASYS^, and leading spectacle lenses.[11,12* **]

IN VITRO DATA SUMMARY

LENS SURFACE WETTABILITY

Contact lens wettability was measured in vitro using the interfacial dewetting and drainage optical platform (iDDrOP) method to assess initial water break-up time for TOTAL30®, AIR OPTIX® plus HydraGlyde®, ULTRA^, ACUVUE VITA^, ACUVUE OASYS^, Biofinity^.[13] This *in vitro* method shows surface wetting properties of different lens materials and is not a clinical performance assessment. With this method, lenses were removed from their blister packs, rinsed and then soaked in phosphate buffered saline (PBS) for approximately 16 hours to remove any blister pack solution. The lenses were then mounted on a curved surface that maintained the shape of the contact lens and then submerged into a PBS bath. The lenses were then raised above the PBS surface while a video recording was taken of the surface of the lenses in order to visualize the dynamic water break-up at the lens surface. The first instance of a break in the lens surface moisture is reported as the surface moisture break-up time.[13] TOTAL30® contact lenses demonstrated a significantly longer surface moisture break up time than AIR OPTIX® plus HydraGlyde®, ULTRA^, ACUVUE VITA^, ACUVUE OASYS^, Biofinity^ ($p<0.001$ for all) meaning that the surface moisture remained intact longer for TOTAL30® (Figure 6).[13]

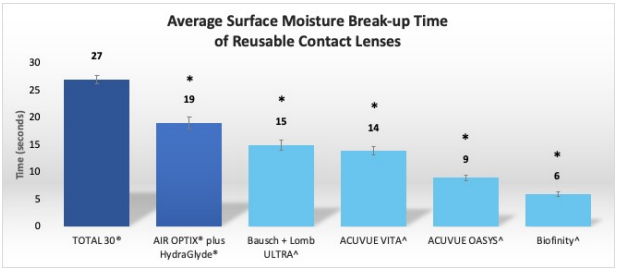


Figure 6: *In vitro* average lens surface moisture break-up time of reusable contact lenses measured by iDDrop method. Surface moisture remained intact on the lens surface longer for TOTAL30® contact lenses as shown by a significantly longer surface moisture break-up time compared to the other reusable lenses ($p<0.05$ for all).[13] Error bars represent standard error.

LENS SURFACE MODULUS

The surface modulus (softness) of reusable contact lenses was measured using atomic force microscopy (AFM) based nanoindentation. All lenses were tested while immersed in PBS solution containing a small amount of surfactant, which is necessary to reduce probe adhesion during the indentation procedure. The AFM probe was pressed against the surface of the lenses with a force applied similar to the eyelid pressure, and the surface modulus was calculated based on the indentation force curve. The softer the material, the lower the surface modulus will be. Measurements were taken of lenses that were either directly removed from their blister pack or after the lens had been worn on-eye for a full wearing schedule (14 days ACUVUE OASYS^; 30 days all other monthly replacement lenses tested). The results of this testing showed that the surface modulus of TOTAL30® contact lenses, for both out of pack and worn lenses, were significantly softer (at least five times softer; $p<0.05$ for all) than worn ACUVUE OASYS^, Biofinity^, ACUVUE VITA^, and ULTRA^ (Figure 7A).[7]

LENS SURFACE LUBRICITY

Surface lubricity testing was performed by measuring the coefficient of friction (CoF) using a Nano-tribometer. Measurements were taken of lenses that were either directly removed from their blister pack or after the lens had been worn on-eye for a full wearing schedule (14 days ACUVUE OASYS^; 30 days all other monthly replacement lenses tested). Lenses were placed on a lens holder and fully submerged in the respective lens packaging solution. A soft probe with force sensors was slid across each lens surface for CoF measurements. TOTAL30® contact lenses maintained their high lubricity even after 30 days of daily wear and demonstrated a significantly lower CoF (at least three times better; $p<0.05$ for all) than worn ACUVUE OASYS^, Biofinity^, ACUVUE VITA^, and ULTRA^, meaning that the surface of TOTAL30® was more lubricious (Figure 7B).[7]

BACTERIA ADHESION

In this in vitro stress testing, unworn contact lenses (TOTAL30®, Biofinity^, ACUVUE VITA^, ACUVUE OASYS^, and ULTRA^) were exposed to separate solutions containing different strains of Pseudomonas aeruginosa. The lenses were also exposed to one strain of Pseudomonas aeruginosa (ATCC 10145) containing green fluorescent protein (GFP) expression. These specific samples were then assessed using microscopy in order to visualize the surface bacterial adhesion on each contact lens brand for this particular strain of Pseudomonas aeruginosa (Figure 8).[6] Quantification of colony forming units (CFU) of five different strains of Pseudomonas aeruginosa (MCC 3478, 3480, 3481, 7142, and ATCC 10145) showed that there was significantly less Pseudomonas aeruginosa adhesion on the surface of TOTAL30® contact lenses ($p<0.0001$ for all) compared to the other lenses tested.[6,7]

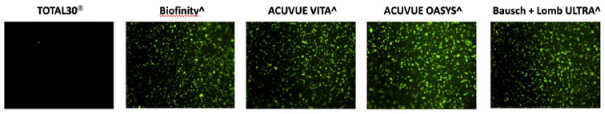
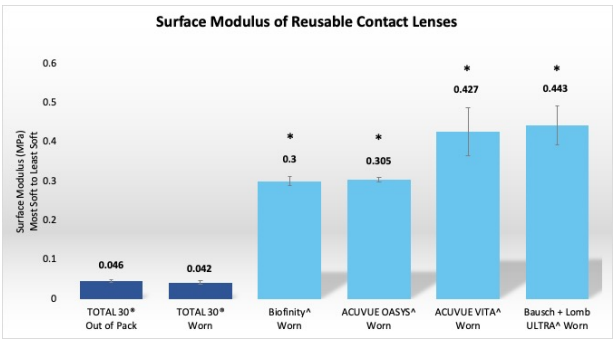


Figure 8: Visualization of surface bacterial adhesion of Pseudomonas aeruginosa (ATCC 10145) on reusable contact lenses. The representative images are based on in vitro stress testing of unworn lenses after exposure to GFP-expressing Pseudomonas aeruginosa (ATCC 10145) and visualized on a microscope (10X magnification).[6]

A



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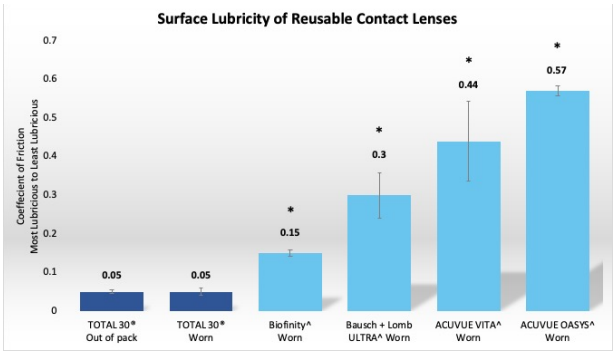

Figure 7: Average lens surface modulus measured with AFM nanoindentation (A) and average coefficient of friction (CoF) measured with nano-tribometer (B). Worn and unworn (out of pack) TOTAL30® contact lenses had a softer ($p<0.05$ for all) and more lubricious ($p<0.05$ for all) surface compared to other reusable lenses that were worn for a full wearing schedule.7 Error bars represent standard error.

LIPID DEPOSITION

Confocal microscopy was used to image the fluorescently labeled non-polar lipid deposition on unworn TOTAL30®, Biofinity^, ACUVUE VITA^, ACUVUE OASYS^, and ULTRA^ contact lenses. A lipid solution containing non-polar lipids, cholesteryl ester (CE) and triglyceride (TAG), was used for this in vitro stress testing of lipid deposition. Lenses went through cycles of lipid exposure and lens cleaning to simulate the approved wearing period for each lens.[7]

Two sets of images were created: 1) of the whole, full diameter contact lens (Figure 9A), 2) cross-sections of the lens showing the outer surface, core, and inner surface (Figure 9B). All images show lipid deposition on the surface and in the core; however, the cross-section images allow for visualization of the surface and core lipids individually (Figure 9). The gray color corresponds to the fluorescence of the lens material and background. The red color corresponds to the fluorescently labeled triglyceride non-polar lipid (Rh-TAG), while the green color corresponds to the fluorescently labeled cholesteryl ester non-polar lipid (TF-CE).[7] Fluorescent intensity measurements showed that lipid deposition on both the whole lens and the surface only was significantly less for TOTAL30® contact lenses compared to the other contact lenses tested ($p<0.01$ for all).[7]

SUMMARY

TOTAL30® (lehfilcon A) contact lenses are the first monthly replacement lenses with Water Gradient Technology. TOTAL30® contact lenses also feature Celligent® Technology which mimics the corneal surface.[5] As demonstrated by *in-vitro* testing, these two unique technologies allow the surface of these lenses to be extremely soft and lubricious and help to resist bacteria and lipid deposits.[6,7,8] TOTAL30® contact lenses bring new technology advancements to the monthly category and are designed to meet the needs of monthly lens wearers.

^trademarks are the property of their respective owners.

*UV-blocking contact lenses are NOT substitutes for protective UV-blocking eyewear such as UV-blocking goggles or sunglasses because they do not completely cover the eye and surrounding area.

**There is no demonstrated clinical benefit to a 34% reduction in visible light at wavelengths below 450 nm.

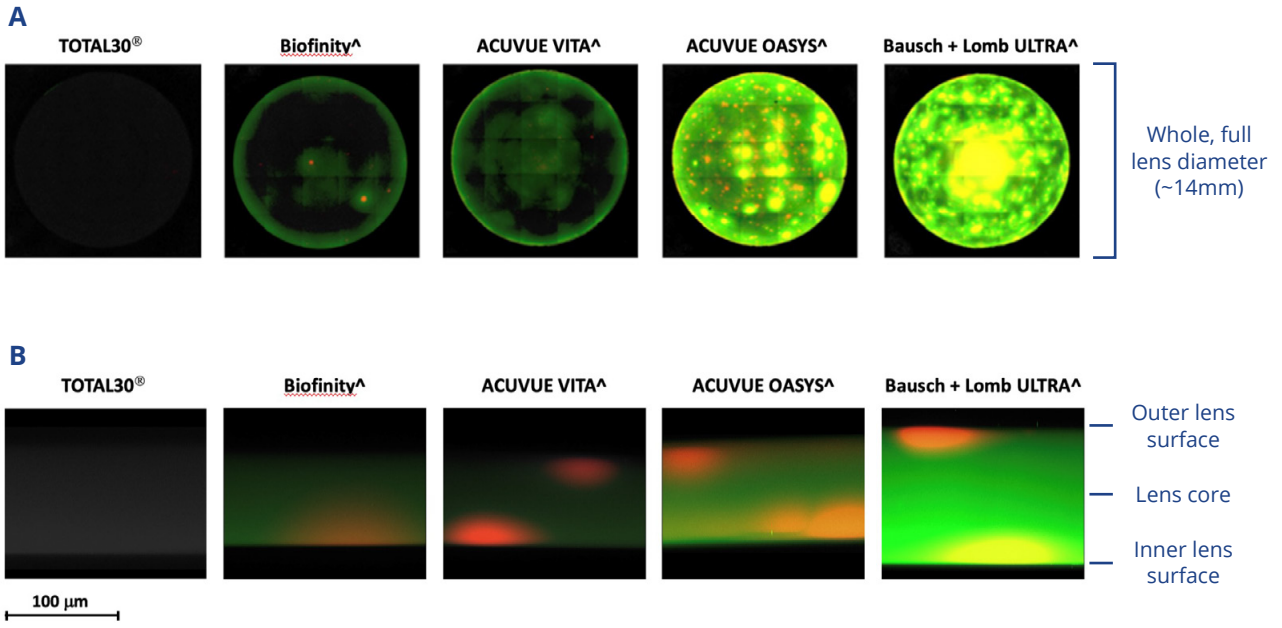

Figure 9: Surface and core lipid deposition on reusable contact lenses. Representative images of *in vitro* stress testing of unworn lenses in A) Whole lens top view imaging and B) Cross section imaging of full thickness lenses after exposure to fluorescently labeled non-polar lipids, cholesteryl ester (CE) and triglyceride (TAG), and visualized on a confocal microscope to show both core and surface lipid deposition .

REFERENCES

1. Morgan PB, Woods CA, Tranoudis JG, et al. International Contact Lens Prescribing in 2020. Contact Lens Spectrum. 2021 (January).
2. Surface characteristics of lehfilcon A contact lenses; Alcon data on file, 2021.
3. Oxygen permeability measurement of lehfilcon A contact lenses; Alcon data on file, 2019.
4. Alcon data on file, 2021.
5. Scanning transmission electron microscopy of lehfilcon A contact lens and human corneal surface; Alcon data on file, 2020.
6. In vitro evaluation of bacterial adherence in commercial lenses; Alcon data on file, 2020.
7. In vitro evaluation of lipid deposition, surface modulus and surface lubricity in commercial lenses; Alcon data on file, 2021.
8. Ishihara K, Fukazawa K, Shi X, Wu J, et al. Antifouling silicone hydrogel contact lenses with bioinspired surface. ACS Omega. 2021; 6: 7058.
9. Ishihara K. Revolutionary advances in 2-methacryloyloxyethyl phosphorylcholine polymers as biomaterials. J Biomed Mater Res Part A. 2019; 107A: 933–943.
10. Shi X, Cantu-Crouch D, Sharma V et al. Surface characterization of a silicone hydrogel contact lens having bioinspired 2-methacryloyloxyethyl phosphorylcholine polymer in hydrated state. Colloid and Surfaces B: Biointerfaces. 2021; 199, 111539.
11. Laboratory assessment of ultraviolet and visible light transmission properties of lehfilcon A contact lenses; Alcon data on file, 2020.
12. Johnson & Johnson Vision Care Professional website. ACUVUE OASYS 2-week contact lenses package insert accessed June 14, 2021. https://www.jnjvisionpro.com/sites/us/files/public/Products/Acuvue_Hydraclear/ao-06-15-01_web_package_insert_and_fitting_guide.pdf
13. In vitro evaluation of lens surface moisture; Alcon data on file, 2021.

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