Updating the Contact Lens Classification System

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- The information presented is only for scientific discussion at the symposium

CDRH's Mission is:

Getting safe and effective devices to market as quickly as possible…

… while ensuring that devices and radiological products currently on the market remain safe and effective.

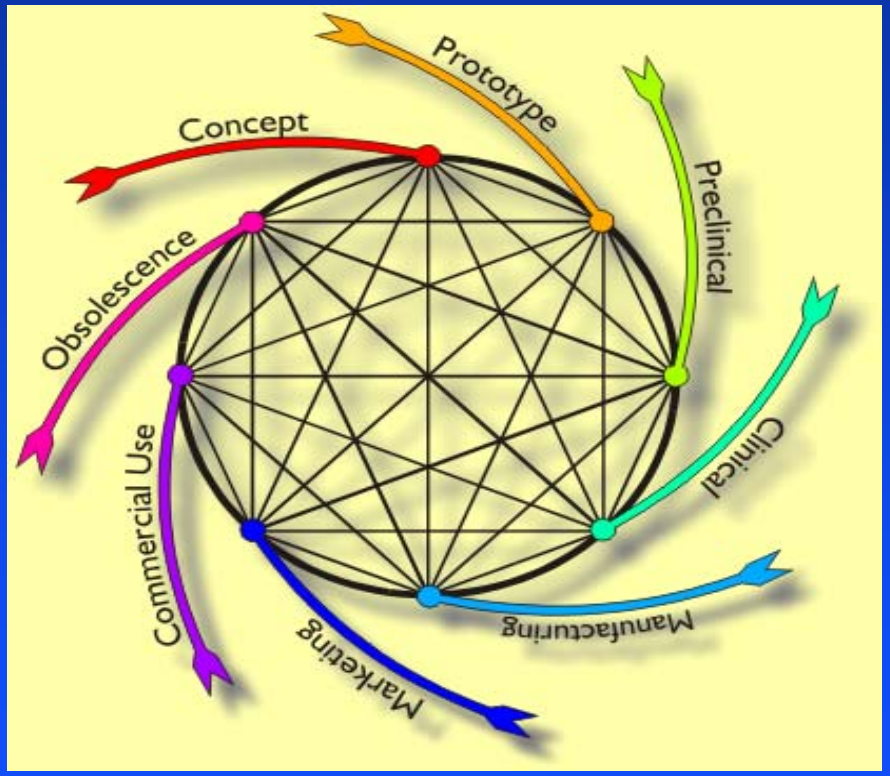
Helping the public get science-based accurate information about medical devices and radiological products needed to improve health

Postmarket Activities

- FDA's job is not over once a device is approved
- We continue to monitor device performance
  - Post-approval studies (in some cases)
  - Mandatory adverse event report system (MDR)
  - Voluntary adverse event report system (MedWatch)

    http://www.fda.gov/medwatch/
  - Annual reports from manufacturers
  - Attendance at scientific/clinical meetings
  - Monitoring the scientific literature

Total Product Lifecycle



Contact Lens Safety

- First Contact Lens approval (March 18, 1971)
- Today - 34 million contact lens wearers in U.S.
- Significant public health impact – FDA safeguards:
  - FDA Guidance for CLs and CL Care Products
  - FDA Website
  - Standards
- Recent Outbreaks
  - 2006 – *Fusarium* keratitis
  - 2007 – *Acanthamoeba* keratitis

Response

Fusarium Keratitis:

B&L MoistureLoc withdrawn (2006)

***Acanthamoeba* Keratitis:**

AMO Complete MoisturePlus withdrawn (2007)

FDA's Response

- Take post-market experience and feed it back into pre-market review process
- Re-assess CL safety and guidance recommendations
  - Identified new concerns due to:
    - Introduction of new lens materials
    - Different care product formulations
    - Greater potential for interaction between CL and CL care products
    - Different patterns of use (as compared to 90's)
      - Does device's margin of safety overcome "misuse"?

Categorization of Silicone Hydrogels History FDA Grouping of Conventional Lenses

July 1985 – FDA Draft Guidelines for Testing Contact Lens Care Products

- Historically lens-solution compatibility was problematic due to both dimensional stability and toxicity/irritation due to adsorbed preservatives
- Each care product was tested with each lens, all tested combinations listed on label
- The 1985 FDA Groupings were developed to categorize lens behavior when used with different care product solutions, as well as lens interactions with proteins in the tear film.

Current FDA Lens Groupings

- Conventional lenses are classified into 4 groups:
  - Group 1 – Nonionic hydrogels <50% water
  - Group 2 – Nonionic hydrogels >50% water
  - Group 3 – Ionic hydrogels <50% water
  - Group 4 – Ionic hydrogels >50% water

Limitations of Current Lens Groupings for Silicone Hydrogels

- Solution and Lens Incompatibilities with Silicone Hydrogels not Predicted by FDA Groups 1-4
  - AMO UltraCare Disinfecting System (peroxide -catalase) with B&L PureVision (balafilcon A) *originally FDA Group 3 (Precaution in labeling)*
  - Ciba SoloCare (PHMB) with Vistakon Acuvue Advance (galyfilcon A) *originally FDA Group 1 (Precaution in labeling, SoloCare no longer marketed)*

Causes of incompatibilities were never determined

Susan J. Gromacki Caring for Silicone Hydrogel Contact Lenses – Part 3, Contact Lens Spectrum, 20(8) Aug 2005 23

Categorization of the Numerous Silicone Hydrogels Lenses

- ISO added one separate grouping/category for all silicone hydrogel lenses
  - ISO Group V – published February 2009, ISO 18369-1

- A single group for all SiHy lens materials is not adequately robust to predict lens-solution incompatibilities
  - Increased potential for lipid uptake
  - Preservative/surfactants adsorption differences
  - Water content
  - Ionic charges
  - Surface treatments

Increasing Complexity of Care Products May Affect Compatibility

Care product formulations are more complex (*more than cleaning and disinfecting lenses)*

- Comfort
- Moisture retention
- Conditioning
- Lubrication

HA Ketelson, DL Meadows, RP Stone, Dynamic Wettability Properties of a Soft Contact Lens Hydrogel, Colloids and Surfaces B; Biointerfaces 40 1-9 (2005)
B Levy, D Heiler, S Norton, Report on Testing from an Investigation of Fusarium in Contact Lens Wearers, Eye & Contact Lens, 32(6) 256-261 (2006)

Categorization of the Numerous Silicone Hydrogels Lenses

- Use experimental data to subgroup lenses based on interaction with MPS solutions
- Compare silicone hydrogels vs. conventional hydrogels in terms of:
  - Free vs. bound water in pores
  - Pore size measurement
  - Preservative uptake/release – maximum adsorption as well as rates
  - Lipid affinity/hydrophobicity
- Update international standards and FDA guidance

Free vs. Bound Water in Pores

Evaluation of Water Content

- Diffusion of preservatives and small molecules through hydrated portion of hydrogel material
- Diffusion complicated by the presence of polymer matrix
- Compare distribution of water states in SiHy vs conventional hydrogel materials
  - Freezable water → mobile
  - Non-freezable water → interaction with hydrogel surfaces

Methods – Water Content

- Use differential scanning calorimetry (DSC) to quantify the states of water
  - Conventional hydrogel lenses
  - SiHy lenses
- Compare distribution of water states between lenses
  - Freezable water vs. total water

Results – Water Content

- Relationship of amount of freezable water in lenses with total water content
  - » Differences in total water for all CL materials are mainly due to freezable water

- Similarity of relationship between freezable and total water content → grouping rules should be applied to both conventional and silicone hydrogels

Pore Size

Evaluation of Pore Size

- Average pore size, pore size distribution, and pore interconnections → limit diffusion of solutes through hydrogel
- Currently unknown extent diffusion of care product components is limited by pore size
- Pore characteristics of hydrogels are difficult to quantify

Methods – Pore Size

- Fluorescent probe permeation method
  - Estimate pore sizes of conventional and silicone hydrogel lenses
- Size of probe occluded by lens material → indicate size of largest set of pores (effective pore size)
- Confocal images → show location of fluorescent probes in lens materials

Results – Pore Size

- Conventional and silicone hydrogel lens materials have generally similar effective pore sizes
- Surface coated SiHy lenses (lotrafilcon A & B) appeared to have smaller effective pore sizes
- Pore sizes are large compared to the size of typical care product components (e.g., PHMB)
- SiHy and conventional hydrogel lenses cannot be differentiated based on pore structure of bulk material

Preservative Uptake

Evaluation of Preservative Uptake

- Preservatives (e.g., PHMB) may be depleted from care products
- Grouping system for conventional lenses have been used to predict preservative uptake
- Preservative uptake and release likely depends on pore size, pore volume, effective charge, and characteristics of silicone phase
  - Surface adsorption - poly(HEMA) and SiHy
  - Bulk absorption – silicone phase in SiHy

Methods – Preservative Uptake

- Measured initial preservative uptake rate and cumulative preservative uptake
  - » Give information regarding the porous structure of lens material
- Initial uptake rates → indicative of pore size and interconnections (effective pore size)
- Cumulative uptake → information regarding total matrix surface area of bulk material
  - » Total matrix surface area, charge, total pore volume, amount of silicone phase

Results – Preservative Uptake

- Charged or high water content lens materials have higher initial PHMB uptake rate vs. uncharged, low water materials
- Surface treatment did not appear to have impact on uptake rate
  - Effective pore size → large compared to size of preservative
- SiHy & poly(HEMA) behave similarly with respect to preservative uptake predictable based on water content & charge
  - silicone phase causes differences in uptake/release of some components

Results – Preservative Uptake

- Cumulative preservative uptake → maximum capacity of lens to absorb preservative
- SiHy lenses show strong correlation between PHMB uptake and high water content or charge
  - similar to conventional hydrogel lenses

Lipid Affinity/Hydrophobicity

Hydrophobicity

Picture courtesy of Nancy Keir. Image obtained from Lorentz et al., 2007

"In general, the biotolerance of these lenses is dictated, at least in part, by the change in comfort affected by irreversibly sorbed molecules. Whether this process is governed by the mechanical action of the deposited debris or from a more complex immune response is not completely understood."
Maziarz et al., 2006

Lipid film and lens calculi on a silicone hydrogel lens after 3 weeks of wear. The patient had previously worn an FDA group IV lens on a 4-weekly replacement period with no such deposition being seen.

Lipid Deposits on Lenses

- Conventional lenses (Bontempo 2001, 6 days daily wear):[1]
  - FDA Group 1 ~3 ug/lens lipid
  - FDA Group 4 ~4 ug/lens lipid
- Silicone hydrogels (Maziarz 2006):[2]
  - 0 - 25 ug/lens lipid (30 days daily wear, balafilcon A, lotrafilcon A, galyfilcon A)
- Typical lens mass = 32 mg

1- cholesterol oleate, cholesterol, oleic acid, oleic acid metyl ester, triolein
2- cholesterol, oleic acid methyl ester, oleic acid

Hydrophobicity

- Uptake of PHMB dependent on charge and water content of lenses
  - Both conventional and SiHy lenses
- Aldox more readily taken up by all SiHy lens materials regardless of charge*
  - PHMB → cationic, hydrophilic
  - Aldox → strong lipophilic, surfactant-like

Charles H. Powell, John M. Lally, Lisa D. Hoong, Stanley W. Huth, Lipophilic versus hydrodynamic modes of uptake and release by contact lenses of active entities used in multipurpose solutions, Contact Lens & Anterior Eye. 23, 9-18 (2010)

Limitations of Current Lens Groupings: Unique Features of Silicone Hydrogels

Conventional poly(HEMA) lenses

- Water filled pores

Silicone hydrogel lenses

- Water filled pores
- Silicone phase
- Surface treatments
- Water soluble polymers - semi-inter-penetrating polymer networks

Categorization of Silicone Hydrogel Lenses

- Current lens groupings are inadequate to evaluate silicone hydrogel incompatibilities
- Proposed groupings will depend on: lens porous structure, ionic charges, lipid affinity/hydrophobic character
- Goal – predict disruption of care product function such as disinfection (preservative depletion), as well as dimensional stability, and other functions

Summary

- Both conventional and SiHy lenses were found to have similar non-freezing water content
  - Freezing water content increased with total water content
  - Amount of water available for diffusion can be grouped according to equilibrium water content
- Effective pore sizes large enough to allow uptake of common preservatives
  - Uptake dependent on water content and charge
  - Effect of surface treatment on preservative uptake minimal

Summary

- Bulk material hydrophobicity of conventional vs. SiHy lens material
- SiHy materials can be grouped similarly to conventional hydrogel lenses
  - Grouping separate from conventional hydrogels because of hydrophobicity of silicone phase

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QUESTIONS

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World Wide Web

http://www.fda.gov/cdrh/devadvice