SCREENING ADHESIVES FOR REUSABLE MEDICAL DEVICES - UPDATE

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THE HISTORY

Adhesives have been used successfully for over twenty-five years in a variety of markets including automotive, general industrial, electronics, and medical. Anaerobic sealants, cyanoacrylates, and light curing acrylics and silicones are used in diverse life-saving applications ranging from automotive airbag sensors to catheters and blood oxygenators. Each industry has different requirements for the selected adhesive ranging from appearance and bond performance to environmental resistance and other parameters.

Over the past two decades, the types of devices, substrates, and sterilization procedures have seen many changes. In the early 1970s, device manufacturers were utilizing materials such as glass, rubber, and metal to assemble syringes, surgical instruments, and other devices. Such materials were assembled with fasteners and/or machined or molded in the appropriate geometries. The devices were typically resistant to rigorous sterilization methods. In the 1980s, as medical technology advanced towards intricate and high performance medical device designs, the need for engineering plastics became apparent. During this same period, a shift to *single use* devices (due to advances of contagious disease) forced design engineers to evaluate engineering plastics such as acrylic, polycarbonate, polysulfone, and PVC. The demands on the adhesive as well as on the plastics selected for these new device designs has challenged suppliers to evaluate their materials against new standards. A long and successful track record exists for these new designs with regards to withstanding sterilization methods such as gamma, EtO, and single cycles of autoclave.

TYPES OF DEVICES

Traditionally, two types of medical devices have been the focus of adhesive manufacturers' involvement in the medical device market: sterile disposable and non-sterile reusables. Sterile disposables are devices such as syringes, catheters and oxygenators which may come in direct contact with blood or bodily fluids. Because of such contact, the requirements for the adhesives used in sterile devices must be thoroughly tested by the manufacturer and must pass stringent toxicity testing. Sterile disposable devices are sterilized by the manufacturer before release and could be potentially re-sterilized at a health-care facility prior to use.

Non-sterile reusables are usually external devices which do not come into direct contact with bodily fluids. Devices such as knee braces, walking aids, and hearing aids would be classified as non-sterile reusables. Typically, materials conducive to long-term use are selected for the construction of such devices, and there are no requirements for toxicity or sterilization resistance.

Sterile reusable devices have seen tremendous growth in recent years due to advances in less invasive surgery. Sterile reusables include surgical equipment such as endoscopes, laproscopes, and surgical instruments. Resposable devices are newly emerging markets in the medical device manufacturing industry. In an effort to reduce costs, medical providers are actively investigating the re-sterilization of surgical instruments - reusables - and the re-sterilization and reuse of devices initially intended for one time use - resposables. New hospital sterilization methods have been introduced (room temperature processing) for some reusables, but most will require substrates and adhesives with increased heat and chemical resistance. These materials must also withstand re-sterilization. It is unknown what the outcome of marketing resposable devices will be in the United States. It is evident, however, that the bar has been raised for more sterilization resistant materials to be used for reusable devices.

THE STUDY

With the emergence of these new classifications of medical devices, Loctite Corporation has outlined a three phase study to examine the effect of repeated sterilization cycles on its medical device adhesives. Phase I was outlined to validate the project and ensure that the existing medical adhesives could withstand repeated cycles. Phase II evaluated select adhesives currently classified as medical device products, and the third phase will identify adhesives with increased temperature resistance. The three phases include:

Phase I:
screen selected cyanoacrylate, light curing acrylics and silicone adhesives and sealants
substrates - polycarbonate, polyetherimide
sterilization methods - autoclave, hydrogen peroxide, glutaraldehyde
sterilization cycles - 10, 50, 100

Phase II:
evaluate select medical device adhesives
substrates - polycarbonate, liquid crystal polymer, polysulfone
sterilization methods - autoclave, hydrogen peroxide, glutaraldehyde
sterilization cycles - up to 50 cycles for all adhesives except autoclave of polycarbonate

Phase III:
identify products with increased temperature resistance
submit products for toxicity testing
add newly compliant products to medical device adhesives line

The following sterilization parameters have been outlined for use in all phases of the study:

Sterilization Method Equipment	Exposure Time/Cycle	Temperature
Autoclave Amsco Century Prevac	6 minutes steam, 3 minutes dry	132°C
3.4 % Glutaraldehyde Johnson & Johnson Cidex Plus	10 hour soak	ambient
Hydrogen Peroxide STERRAD™ System	15 minute plasma	40 - 45°C

STERILIZATION METHODS

Sterilization is defined as the complete destruction of all bacteria and/or infectious organisms in a product (*The Condensed Chemical Dictionary, 10th Edition*). Prior to the undertaking of the three phase study, the medical adhesives in this study had been tested after limited exposure to various sterilization environments: three cycles of ethylene oxide (EtO), up to 7.5 megarads of gamma radiation, one cycle of autoclave (sterilization methods typical of the medical device manufacturing industry). Evaluations of adhesive performance after exposure to extended autoclave, hydrogen peroxide and glutaraldehyde were the target of the three phase study.

Of the sterilization methods mentioned, steam autoclaving is the most widely used on these types of devices, accounting for approximately 80% of all medical device sterilization. Due to its ease of use, lack of toxic by-products, short cycle time, and high effectiveness, steam autoclaving is expected to continue to be the sterilization of choice for the near future. A typical autoclave cycle involves temperatures up to 121 - 132°C for four to six minutes, followed by a cool/dry cycle.

EtO sterilization is commonly used by medical device manufacturers as well as medical providers for devices which cannot withstand the extreme steam environment of the autoclave. Several limitations exist when working with EtO systems including the storage/use of a toxic gas, the high cost associated with the EtO systems, and the need for sterilized devices to be aerated for up to twenty-fours hours to ensure complete dissipation of toxic residues. EtO exposure parameters vary from user to user.

Glutaraldehyde exposure is classified as a chemical sterilization method. The most significant limitation of chemical sterilization methods such as glutaraldehyde is the time required for complete sterilization. A typical cycle of glutaraldehyde sterilization requires a ten hour soak, followed by a water rinse.

Due its ease of use, lack of toxic residues, and quick cycle times, hydrogen peroxide sterilization has the potential to replace many of the commonly used methods such as autoclaving and EtO. Because hydrogen peroxide is environmentally safe, devices are not required to be rinsed nor stored for full aeration of toxic residues. The current limitation of hydrogen peroxide sterilization lies in the capital costs associated with acquiring the necessary equipment. A typical hydrogen peroxide sterilization cycle consists of a fifteen minute plasma phase at 40 - 45°C.

PHASE I RESULTS:

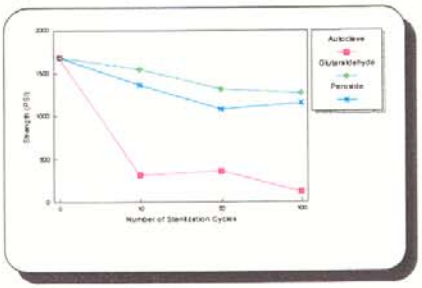
For the preliminary screening of Loctite adhesives to repeated sterilization, two substrates were selected based on market input and reported sterilization resistance: polycarbonate and polyetherimide. The following medical adhesives and substrates were evaluated:

Adhesive Family	Status	Substrate Tested
Light Curing Acrylic Adhesive	USP Class VI compliant Cytotoxicity, hemolysis tested	polycarbonate to polycarbonate polyetherimide to polycarbonate
Surface Insensitive Cyanoacrylate Adhesive	USP Class VI compliant Cytotoxicity, hemolysis tested	polycarbonate to polycarbonate polyetherimide to polyetherimide
Thermal Cycling Cyanoacrylate Adhesive	USP Class VI compliant Cytotoxicity, hemolysis tested	polycarbonate to polycarbonate polyetherimide to polyetherimide
Light Curing Silicone	USP Class VI compliant Cytotoxicity, hemolysis tested	cured adhesive film

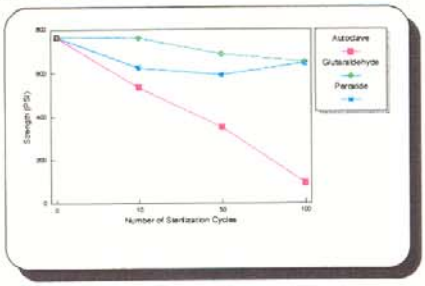
Adhesives were tested on modified lapshears of the designated plastic, with the exception of the light curing silicone which was tested as a cured film. Assemblies designated for sterilization were exposed to 10, 50, and 100 cycles of autoclave, hydrogen peroxide, or glutaraldehyde and compared to control samples. Sterilization cycle parameters were as previously listed under *The Study*.

The performance results for the four adhesives evaluated in Phase I validated the theory that Loctite adhesives could withstand numerous cycles of the selected sterilization methods. Figures 1 and 2 below provide the results for the light curing acrylic adhesive on polycarbonate and polyetherimide lapshears, exposed to a maximum of 100 cycles of autoclave, glutaraldehyde or hydrogen peroxide. As indicated, the adhesive maintained approximately 85% of its initial strength after 100 cycle exposure to either glutaraldehyde or hydrogen peroxide. Autoclaving proved to be the most rigorous environment, causing bond strengths to drop off significantly, particularly on polycarbonate lapshears. Because several grades of polycarbonate are known to resist minimal autoclave cycles (i.e. ten cycles), the low bond strengths noted following autoclave exposure may be a result of a change in the plastic rather than adhesive degradation.

Figures 1 and 2
Light Curing Acrylic Adhesive on Polycarbonate and Polyetherimide



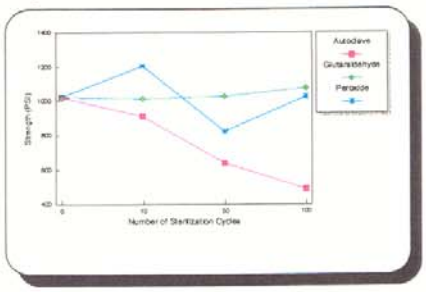
Light Curing Acrylic on PC



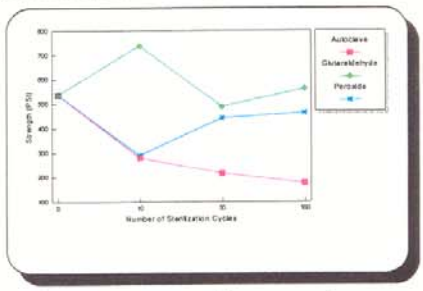
Light Curing Acrylic on Polyetherimide

Figures 3 and 4 provide the results obtained for the repeated sterilization of polycarbonate and polyetherimide assemblies using the Surface Insensitive cyanoacrylate adhesive. No significant effect was noted on bond performance after 100 cycles of either hydrogen peroxide or glutaraldehyde, although all polycarbonate assemblies did exhibit substrate failure. A decrease of approximately 50% was noted for all assemblies exposed to 50 cycles of autoclave sterilization - regardless of the plastic substrate. Because of the difficulty in achieving initial high bond strengths on polyetherimide, the declining trend noted following autoclave exposure may not be representative of adhesive degradation alone. A trend, similar to that noted for the light cure acrylic adhesive polycarbonate assemblies exposed to 50 plus cycles of autoclave, was recorded for the Surface Insensitive cyanoacrylate on polycarbonate. All assemblies exhibited substrate failure and the values, therefore, are not a true representation of adhesive performance.

Figures 3 and 4
Surface Insensitive Cyanoacrylate Adhesive on Polycarbonate and Polyetherimide



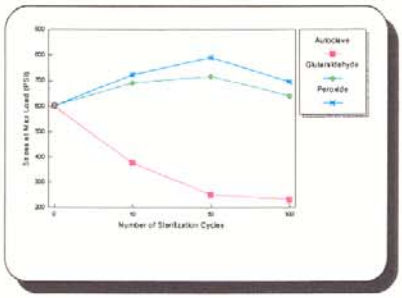
Surface Insensitive Cyanoacrylate on PC



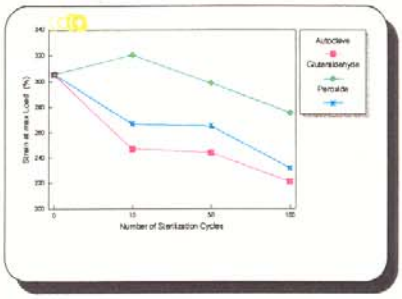
Surface Insensitive Cyanoacrylate on Polyetherimide

Sterilization exposure of the cured film of the light curing silicone resulted in a slight decrease in percent elongation, but all values remained above 200%. Effect on tensile strength was negligible for hydrogen peroxide and glutaraldehyde sterilization exposure. Exposure to autoclave sterilization, however, resulted in a slightly greater than 50% drop in tensile strength values. Figures 5 and 6 provide these results graphically.

Figures 5 and 6
Light Curing Silicone Tensile and % Elongation



Light Curing Silicone Tensile Strength



Light Curing Silicone % Elongation

PHASE I SUMMARY

Several conclusions can be drawn from the preliminary screening of adhesives and substrates conducted in Phase I of this study. The selected adhesives and substrates maintained performance after 100 cycles of immersion in liquid sterilants such as glutaraldehyde. Similarly, exposure of the polycarbonate, polyetherimide and cured film samples to hydrogen peroxide sterilization showed little change after 100 cycles of exposure. Exposure to autoclave sterilization proved to be the most rigorous - resulting in declining performance across the three adhesive categories. Because of the noted substrate failures for autoclaved polycarbonate assemblies and the initially low bond strengths obtained with polyetherimide, the use of more than ten autoclave cycles needs to be reevaluated.

The Phase I data indicates that the three adhesive families examined - light curing acrylic, cyanoacrylate, and light curing silicone - all have potential for reusable and resposable devices. The substrates used, bond configuration, and sterilization type and duration must all be taken into account when designing a device that is targeted for repeated sterilization.

PHASE II

Based on the data collected in Phase I, Phase II of Loctite's adhesive screening project encompassed the majority of its medical products. A recent survey of medical device manufacturers producing sterile disposable and potentially reusable devices indicated that plastics of choice currently include polycarbonate, liquid crystal polymer, and polysulfone. Therefore the following adhesives and substrates were identified for this second phase study:

Adhesive Family	USP Class VI Status	Substrate Tested
Seven Light Curing Acrylic Adhesives	USP Class VI compliant Cytotoxicity, hemolysis tested	polycarbonate to polycarbonate polysulfone to polysulfone
Ten Cyanoacrylate Adhesives	USP Class VI compliant Cytotoxicity, hemolysis tested	polycarbonate to polycarbonate liquid crystal polymer to liquid crystal polymer

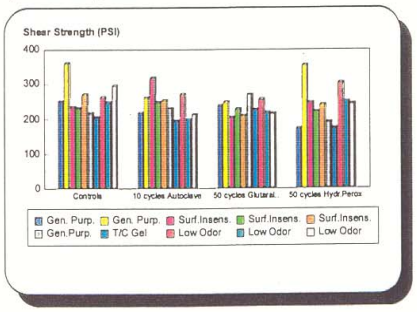
As with Phase I, the listed adhesives underwent autoclave, hydrogen peroxide, and glutaraldehyde sterilization. The exposure of polycarbonate assemblies in the autoclave was limited to a maximum of 10 cycles due to the first phase results (i.e. substrate failure and/or rapidly decreasing values). The goal of Phase II of Loctite's repeated sterilization study is to test all products to a minimum of 50 cycles of each sterilization method with the exception of the aforementioned 10 cycles of autoclave.

PHASE II RESULTS

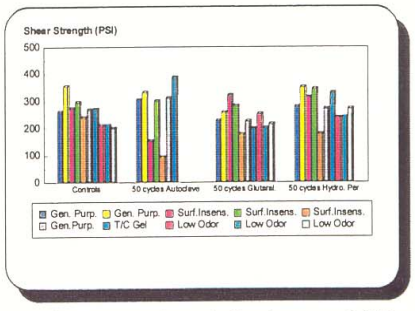
Figures 7 and 8 provide the results for the ten cyanoacrylate adhesives evaluated on polycarbonate as well as liquid crystal polymer. Polycarbonate assemblies (see Figure 7) exposed to ten (10) cycles of autoclave, fifty (50) cycles of liquid sterilant immersion, or fifty (50) cycles of hydrogen peroxide did not exhibit significant changes in shear strengths.

The performance trends for cyanoacrylate adhesives evaluated on liquid crystal polymer are provided in Figure 8. The ten cyanoacrylate adhesives performed well overall, with the majority of assemblies maintaining initial strength following exposure to fifty (50) cycles of steam, liquid or plasma phase sterilization. Two Surface Insensitive products exhibited a significant decrease in strength following exposure to fifty (50) cycles of autoclave, and the three low odor products resulted in failure following the same autoclave exposure.

Figures 7 and 8
Cyanoacrylate Adhesives on Polycarbonate and Liquid Crystal Polymer (LCP)



Cyanoacrylate Adhesives on Polycarbonate

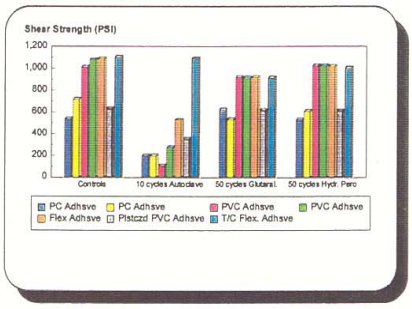


Cyanoacrylate Adhesives on LCP

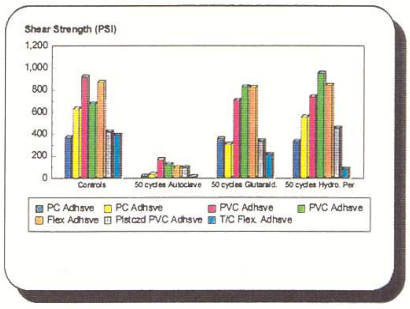
The phase II results obtained for seven (7) light curing adhesives are provided in Figures 9 and 10. Evaluation of light curing adhesives on polycarbonate following exposure to ten (10) cycles of autoclave, fifty (50) cycles of liquid sterilant immersion, or fifty (50) cycles of hydrogen peroxide are shown in Figure 9. With the exception of a thermal cycling, flexible, acrylic adhesive, the remaining six (6) light curing adhesives exhibited a significant decrease in shear strength following exposure to ten (10) autoclave cycles. Exposure of polycarbonate assemblies to fifty (50) cycles of either liquid glutaraldehyde sterilant or fifty (50) cycles of plasma phase hydrogen peroxide resulted in no significant change in shear strengths.

Figure 10 provides the results obtained for the light curing adhesives on polysulfone. All products were significantly affected by exposure to 50 cycles of steam sterilization. Polysulfone assemblies utilizing the thermal cycling, flexible acrylic adhesive exhibited a decrease in strength of approximately 50% or greater following exposure to fifty (50) cycles of glutaraldehyde and/or hydrogen peroxide. In addition, one of the high viscosity polycarbonate adhesives exhibited a significant decrease in shear strength following exposure to fifty (50) cycles of liquid sterilant.

Figures 9 and 10
Light Curing Adhesives on Polycarbonate and Polysulfone



Light Curing Adhesives on Polycarbonate



Light Curing Adhesives on Polysulfone

PHASE II SUMMARY

The testing completed for the phase II portion of the screening study indicated that exposure to fifty (50) cycles of a liquid sterilant, such as glutaraldehyde, had no overall effect on cyanoacrylate assemblies regardless of whether the substrate was polycarbonate or liquid crystal polymer. Similar results were obtained for the light curing adhesives with the exception of two products evaluated on polysulfone, which were affected by the submersion in glutaraldehyde.

Fifty (50) cycles of hydrogen peroxide sterilization also appeared to have no significant effect on cyanoacrylate assemblies - polycarbonate or liquid crystal polymer - and affected only one of the light curing adhesives on polysulfone specimens.

Autoclaving, as with phase I screening evaluations, proved to be the most aggressive sterilization environment. Several of the cyanoacrylate assemblies involving liquid crystal polymer resulted in a significant decrease in shear strengths following fifty (50) cycles of autoclave exposure - the low odor/bloom products failing during sterilization and two of the surface insensitive products exhibiting a decrease of approximately 50 %. Steam sterilization exhibited the greatest overall effect on the light curing adhesives regardless of substrate, with all products except the toughened, thermal cycling acrylic evaluated on polycarbonate exhibiting a greater than 50% drop off in strength.

PHASE III

Based on the phase I screening data as well as the results obtained from the phase II evaluations, the third phase of the Loctite Reusable Study has been modified. Since steam sterilization proved to be the most rigorous environment for both the light curing adhesives and the cyanoacrylate materials, the project direction has shifted to identifying products with increased temperature resistance - such as epoxy materials and modified acrylics. The newly selected adhesives will be screened first for sterilization resistance. Once successful resistance to repeated cycles is demonstrated, the selected adhesives will be submitted for toxicity testing and added to the existing medical device adhesives line.

SPECIAL THANKS

Special thanks is extended to the following contributors to this study:

- Erin Yaeger of Loctite Corporation for conducting and compiling the Phase I data
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- G.E. Plastics for supplying Lexan® (*polycarbonate*) samples
- Amoco Polymers for supplying Udel® (*polysulfone*) samples
- Hoescht Celanese for supplying LCP (*liquid crystal polymer*) samples
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