CIDEX™ OPA SOLUTION

EFFECTIVENESS AGAINST DISEASE-CAUSING MICROBES

MAIN POINTS

- Five studies have evaluated the effectiveness of CIDEX™ OPA Solution against:
  - ✓ More than 200 strains of bacteria, including antibiotic-resistant strains
  - ✓ Mycobacteria
  - ✓ Spore-forming bacteria
  - ✓ Viruses (CIDEX™ OPA has been directly tested against HUMAN CORONAVIRUS, and has been demonstrated to be effective)
  - ✓ Fungi[1-5]
- CIDEX™ OPA Solution kills everything tested except spores very quickly, even under rigorous testing.[1-5]
- CIDEX™ OPA Solution remains effective in the presence of blood and organic matter.[2, 3]

PURPOSE

The purpose of this document is to provide a review of scientific findings on the killing efficacy of CIDEX™ ortho–phthalaldehyde (OPA) Solution. Five research studies have been reviewed and summarized. Several additional sources were used to provide background information.

Introduction and Background

Healthcare-Associated Infections

Every year, more than 2 million healthcare-associated infections occur in the U.S.[6] These infections result in approximately 90,000 deaths each year, and are one of the most frequent "adverse medical events" in the U.S.[6, 7]

> **A comprehensive review of the medical literature suggests that transmission of infection resulting from gastrointestinal endoscopy is an extremely rare event, and has invariably been associated with a breach in cleaning protocols or defective equipment."[8]**

CIDEX™ OPA SOLUTION

CIDEX™ OPA Solution is a high-level disinfectant (HLD) with low odor and is highly compatible with medical materials.[1, 2, 9] It was developed by Johnson & Johnson Medical Inc. and cleared for use in the U.S. in 1999.9 Scientists have studied the effectiveness of CIDEX™ OPA Solution and have found it to be effective at killing a broad spectrum of bacteria and other disease-causing organisms.[1-5, 9-11]

STUDY METHODS

While the exact testing methods varied between studies, the same general steps were taken in all five research studies.

1. Disease-causing microorganisms (microbes) were obtained either from stock laboratory supplies or from hospitalized patients.
2. Microbes were grown.
3. Microbes on inoculated carriers or in suspension were exposed to CIDEX™ OPA Solution for a set amount of time.
4. Tests were performed to measure microbe survival after exposure to CIDEX™ OPA Solution.[1-5]

LOG_{10} REDUCTIONS

The effectiveness of HLD is often measured in log_{10} reduction factors.[1, 3-5]

To illustrate the concept of log_{10} reduction factors, imagine that there are 5 million bacteria contaminating a medical instrument.

- If disinfected with an HLD with a log_{10} reduction factor of 5.0, 50 bacteria will remain
- If disinfected with an HLD with a log_{10} reduction factor of 4.0, 500 bacteria will remain
- If disinfected with an HLD with a log_{10} reduction factor of 3.0, 5,000 bacteria will remain

In other words, a one-unit increase on the log_{10} scale indicates an increase in killing effectiveness of 10 times.

CIDEX™ OPA SOLUTION EFFECTIVENESS AGAINST VEGETATIVE BACTERIA

The effectiveness of CIDEX™ OPA Solution has been tested against many vegetative bacteria.
See Table 1.

Table 1.
Vegetative Bacteria Killed by CIDEX™ OPA Solution

Acinetobacter baumanii
Acinetobacter species unspecified
Enterobacter cloacae isolated from a patient
Enterobacteriace isolated from a patient
Enterococcus faecalis
– Laboratory strain
– Isolates from patients
Escherichia coli
– 2 laboratory strains
– Isolates from patients
Helicobacter pylori
– 2 laboratory strains
Klebsiella pneumoniae
Proteus mirabilis
Pseudomonas aeruginosa
– 2 laboratory strains
– Isolates from patients
Serratia marcescens
Staphylococcus species unspecified
Staphylococcus aureus
–2 laboratory strains
– Isolates from patients
Stentrophomonas maltophilia
Streptococcus species unspecified
Staphylococcus epidermidis
Xanthomonas maltophilia

In three studies, CIDEX™ OPA Solution was highly bactericidal against all vegetative, non-spore forming microbes.[1, 2, 4]

In two studies by Herruzo-Cabrera, both laboratory stock strains and patient-isolated strains of bacteria were utilized, and CIDEX™ OPA Solution was able to reduce the bacterial load by greater than 10,000 times (log10 reduction factors of 4.63 and 4.7) within 10 minutes.[1, 4]

According to Akamatsu, CIDEX™ OPA Solution eliminated all viable cells for 11 different strains of bacteria in 15 seconds or less.[2] In addition, CIDEX™ OPA Solution remained bactericidal and fast-acting in the presence of human serum for all of the 11 organisms tested.[2]
Another study was designed to represent a "worst case scenario" by using:
• Rough-surfaced instruments.
• Inoculating the instrument with both lab and freshly isolated strains of bacteria and fungi from ICU patients.
- Over 200 strains were tested, including 66 strains of P. aeruginosa, some of which were resistant or multiple drug-resistant
- P. aeruginosa can cause respiratory infections in patients who have endoscopy procedures, and it can often survive high-level disinfection.[1]

CIDEX™ OPA Solution easily killed all of the microbes tested with the exception of P. aeruginosa. While OPA was not able to kill all of the P. aeruginosa strains, it was still able to effectively kill 77% of 44 clinical isolates after 10 minutes of exposure.[1]

When CIDEX™ OPA Solution was compared to other HLDs, CIDEX™ OPA Solution was often faster and more effective.
• In one study, CIDEX™ OPA Solution was twice as fast as glutaraldehyde (GTA) at eliminating 11 strains of bacteria.[2]
• In another study, CIDEX™ OPA Solution killed a higher percentage of microbes than Perasafe (92% vs. 74%).[4] (see Figure 1)

Percent of 54 Microbial Species Completely Killed by HLD Sorce: Herruzo-Cabrera et al. (2006)

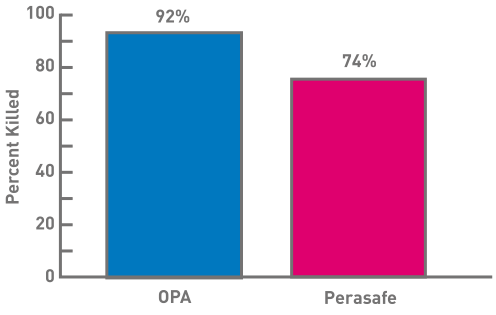

Figure 1. Percent of species killed by CIDEX™ OPA Solution and Perasafe

CIDEX™ OPA SOLUTION EFFECTIVENESS AGAINST MYCOBACTERIA

> **CIDEX™ OPA, at a concentration of 0.55%, shows excellent mycobactericidal activity within 10 min... In comparison, 2% GTA requires at least 20 min to be effective (this time period is even longer for some mycobacteria, e.g. M. avium intracellulare).These findings would vindicate substitution of 2% GTA with 0.55%"[1]**

CIDEX™ OPA SOLUTION EFFECTIVENESS AGAINST MYCOBACTERIA

Figure 2. Close-up of a Mycobacterium tuberculosis growth
Image Source: Public Health Image Library

Mycobacteria cause healthcare-related infections.[3] M. tuberculosis infections can occur from improperly disinfected endoscopes and bronchoscopes. In addition, M. chelonae has been implicated in hospital-acquired infections.[3]

CIDEX™ OPA Solution has been shown to kill mycobacteria in multiple studies.[1, 3, 4]

→ In one study:
- CIDEX™ OPA Solution reduced the number of mycobacteria by a factor greater than 10,000 (log10 reduction factor of 4.3) after 10 minutes of exposure.[4]
- CIDEX™ OPA Solution was more effective at killing mycobacteria than Perasafe.[4]

→ In another study, CIDEX™ OPA Solution was shown to be faster acting against mycobacteria than GTA.[3] (See Figure 3)

Time to Kill Mycobacteria Species by HLD under "Clean" Conditions (without serum)

(Source: Fraud et al. (2001)

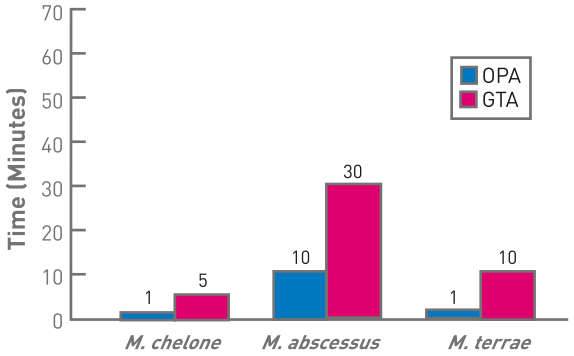

Figure 3. Killing time of Mycobacteria by CIDEX™ OPA Solution and GTA in "clean" conditions

The addition of serum did not affect the efficacy of CIDEX™ OPA Solution against the tested mycobacteria.[2, 3] It did, however, increase the amount of time required for GTA disinfection, doubling the required time for two of the species.[3] (See Figure 4).

Time to Kill Mycobacteria Species by HLD under "Dirty" Conditions (without serum)

(Source: Fraud et al. (2001)

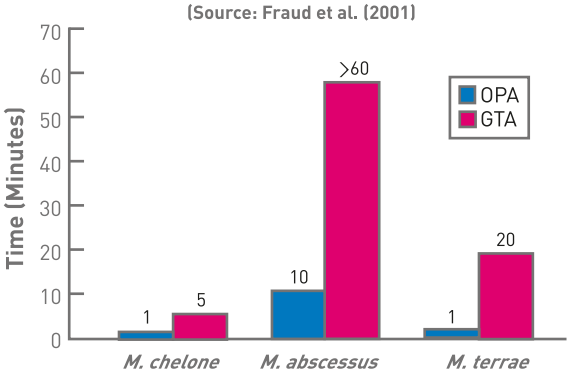

Figure 4. Killing time of Mycobacteria by CIDEX™ OPA Solution and GTA in "dirty" conditions

> **Results showed that 0.5% acidic and alkaline CIDEX™ OPA were rapidly mycobactericidal, under both 'clean' and 'dirty' conditions, and more importantly were active against GTA-resistant strains."[3]**

CIDEX™ OPA SOLUTION EFFECTIVENESS AGAINST SPORES AND VIRUSES

The effectiveness of CIDEX™ OPA Solution has been tested against several mycobacteria.
See Table 2.

Table 2
Mycoacteria Killed by CIDEX™ OPA Solution

Mycobacterium abscessus
M. avium
– 2 laboratory strains
– a patient isolate
M. chelonae
– Laboratory strain
– a patient isolate
– 2 Laboratory strains resistant to GTA
M. fortuitum
– 2 laboratory strains
M. kansasii
M. smegmatis
M. terrae
M. tuberculosis
– 2 laboratory strains

CIDEX™ OPA Solution can also kill GTA-resistant mycobacteria, such as M. chelonae (Epping) and M. chelonae (Harefield).3 These organisms were eliminated by CIDEX™ OPA Solution within two minutes or less in both clean and dirty conditions.[3]

CIDEX™ OPA SOLUTION EFFECTIVENESS AGAINST SPORES AND SPORE-FORMING BACTERIA

Because HLDs are not required to eliminate spores (only sterilization completely eliminates spores9),there are limited data about the efficacy of CIDEX™ OPA Solution against them. The effectiveness of CIDEX™ OPA Solution has been tested against the two spore-forming bacteria.

Figure 5. An electron micrograph of Bacillus subtilis cells

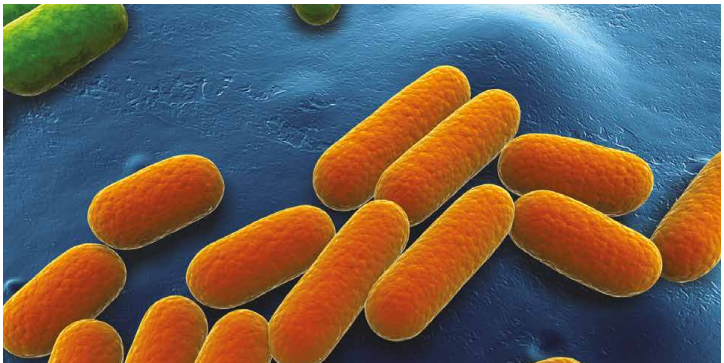

Table 3
Spores Reduced by CIDEX™ OPA Solution

Bacillus subtilis
Bacillus atrophaeus

According to researchers, CIDEX™ OPASolution has shown effectiveness in reducing the number of Bacillus atrophaeus and B. subtilis spores.[4, 9]

Currently, there is great concern about hospital- acquired Clostridium difficile (or "C. diff" as it is called) infections. C. difficile spores are quite sensitive to standard disinfection processes and are eliminated with relatively short times of exposure to HLDs, such as CIDEX™ OPA Solution.[11]

CIDEX™ OPA SOLUTION EFFECTIVENESS AGAINST VIRUSES

Scientists have tested and found CIDEX™ OPA Solution to be virucidal for many viruses.10 Independent researchers have also tested the effectiveness of CIDEX™ OPA on Hepatitis B and Adenovirus [8.2, 5]

Table 4
Viruses Destroyed by CIDEX™ OPA Solution

Adenovirus 2
Adenovirus 8
Coxsackie Type B-3
Cytomegalovirus
Hepatitis B (HBV)
Herpes Simplex 1 and 2
HIV-1
Human Coronavirus
Influenza Type A (Hong Kong)
Polio 1
Rhinovirus Type 42
Vaccinia (smallpox)

HEPATITIS B (HBV)

In one study, scientists used radioimmunoassay to determine if the HBV remained infectious after exposure to CIDEX™ OPA Solution.[2] After 30 seconds, CIDEX™ OPA Solution had reduced the infectivity of HBV below the threshold value for the test.[2]

CIDEX™ OPA SOLUTION EFFECTIVENESS AGAINST FUNGI

> **The World Health Organization recommends hypochlorous acid and GTA as an effective disinfectant against hepatitis B virus; our results show that OPA is also an effective disinfectant against hepatitis B virus."[2]**

ADENOVIRUS 8

Adenovirus 8 is a very resilient virus and can persist in the environment on hard surfaces for more than 30 days.5 It is a common cause of hospital-acquired eye infections and can be spread by:

- Contact with contaminated medical equipment
- Direct person-to-person contact
- Airborne droplets

CIDEX™ OPA Solution was able to reduce the viral load of Adenovirus 8 to safe levels after one minute of exposure, even in the presence of serum. CIDEX™ OPA Solution was also more effective on Adenovirus 8 after exposure for five minutes than all other germicides tested, including peracetic acid and 70% ethanol.[5] (See Figure 6).

Effectiveness of HLDs Against Adenovirus 8
Source: Rutala et al. (2006)

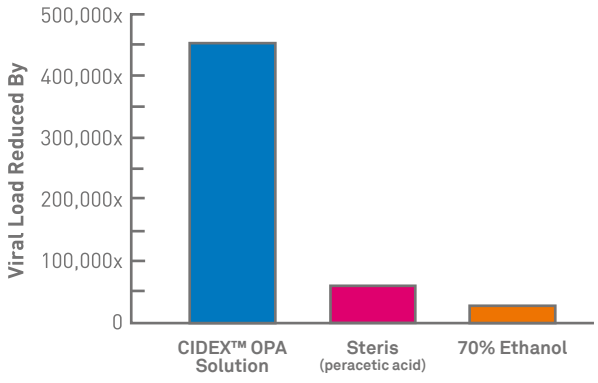

Figure 6. The number of Adenovirus 8 eliminated by three HLDs

CIDEX™ OPA SOLUTION EFFECTIVENESS AGAINST FUNGI

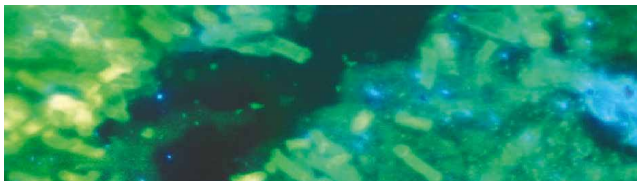

Figure 7. An electron micrograph of Candida albicans
Image Source: Public Health Image Library

The effectiveness of CIDEX™ OPA Solution has been tested against several fungi.

Table 5
Fungi Killed by CIDEX™ OPA Solution

Candida albicans
Mucor racemosus
Rhizopus nigricans
Aspergillus niger
A. terreus

The results of two studies show CIDEX™ OPA Solution as an effective and fast-acting fungicide.[1,2]
Herruzo-Cabrera et al. tested the effect of CIDEX™ OPA Solution on eight different isolates of Candida albicans.1 After 10 minutes of exposure, CIDEX™ OPA Solution reduced the number of organisms by an average of nearly 20,000 times (log10 reduction factor of 4.3).[1]
Akamatsu et al. tested the fungicidal activity of CIDEX™ OPA Solution and GTA against five fungi.2 CIDEX™ OPA Solution was at least twice as fast at killing the fungi tested as GTA.2 (See Figure 8)

Killing Time of OPA and GTA for Fungi in the Presence of Serum
Source: Akamatsu et al. (2005)

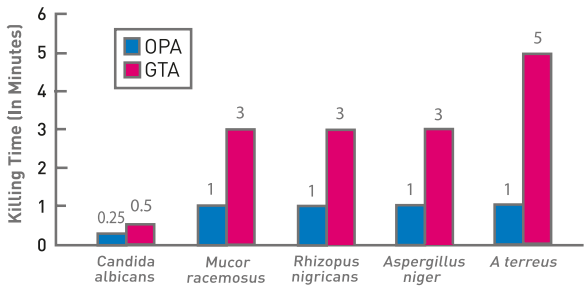

Figure 8. Fungal Killing times by CIDEX™ OPA and GTA in the presence of serum

CIDEX™ OPA SOLUTION : DISCUSSION AND CONCLUSIONS : REFERENCES

DISCUSSION AND CONCLUSIONS

CIDEX™ OPA Solution has demonstrated high levels of bactericidal, virucidal, and fungicidal activity in multiple studies against a wide range of organisms.[1-5, 9]

Clinically isolated bacteria should be used when determining the effectiveness of an HLD because of their increased resistance to HLDs.[1] When CIDEX™ OPA Solution was used against the clinically isolated strains, it was effective against the majority of the tested organisms, even under "worst case" conditions.[1]

There have been limited published studies of the effectiveness of CIDEX™ OPA Solution against viruses. In some cases, it is impossible to do direct virucidal testing because the viruses currently cannot be grown in a laboratory setting (such as human papillomavirus, and Norwalk and Norwalk-like viruses).[9] However, some of the most concerning viruses (such as hepatitis B and C and HIV) are very fragile and are easily destroyed by all HLDs.[11] CIDEX™ OPA Solution was very effective at eliminating Adenovirus 8, a very hardy and persistent virus.[5]

CIDEX™ OPA Solution shows fast killing action against microbes that are resistant to GTA, in addition to having other advantages over GTA.[3]

> **"CIDEX™ OPA Solution has several potential advantages compared to Glutaraldehyde. It has excellent stability over a wide pH range (pH 3-9), is not a known irritant to the eyes and nasal passages, does not require exposure monitoring, has a barely perceptible odor, and requires no activation." [9]**

Post-gastrointestinal endoscope infection occurs very rarely, and has been highly correlated with a break in disinfection procedures or faulty equipment.[8] The scientific evidence shows that CIDEX™ OPA Solution is an easy to use HLD and is very effective.[1, 2, 9]

Although the data used in these papers suggest that CIDEX™ OPA Solution is effective with exposure conditions different than the cleared claims, CIDEX™ OPA Solution should always be used consistent with its Direction for Use.

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FOR TECHNICAL INFORMATION ON CIDEX™ OPA SOLUTION, CONTACT YOUR LOCAL ASP REPRESENTATIVE.

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