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Zentralstelle der Länder
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bei Arzneimitteln
und Medizinprodukten
ZLG-P-429.08.10

Final test report O08ML710H
submitted to

Cavex Holland BV
B.O.Pox 852
NL 2003 RW Haarlem

Evaluation of the effectiveness of

CAVEX ImpreSafe

against

Herpes Simplex Virus type 1

Test method following the guideline of DVV and RKI
dating 01.08.2008

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Test report number # O08ML710H

1. Identification of test laboratory

MikroLab GmbH, Norderoog 2, D-28259 Bremen

2. Identification of sample

Name of product	CAVEX ImpreSafe
Manufacturer	Cavex Holland BV
Application	disinfection of dental impressions
Lot no.	00878
Expiry date	-
substance(s) and concentration(s) in 100 g	30 g benzalkonium chloride
Appearance and odour	clear, blue liquid; product specific
pH-value (s) (in hard water)	undiluted: 8.32 (20°C)
Conditions of storage	room temperature in the dark (area with limited access)
Date of receipt at laboratory	17.11.2008

3. Materials

3.1 Culture medium and reagents

- Dulbecco´s Modified Eagle´s Medium (DMEM, Lonza Group Ltd., catalogue no. BE12-707F)
- fetal calf serum (Biochrom AG, article no. S 0115)
- formaldehyde (Chemisch-technologisches Laboratorium Dr. Melzer, D-28199 Bremen)
- Aqua bidest. (Fresenius Kabi Deutschland, article no. P2N 1636071)
- PBS (Invitrogen, article no. 18912-014)

3.2 Virus and cells

Herpes Simplex Virus type 1 prototype strain Kupka originated from the Department of Virology and Antiviral Therapy, Universitätsklinikum Jena, D-07740 Jena. Before inactivation

assays, virus had been passaged in *Rabbit Primary Kidney Cells (RTP)* and 3-5 times in *BGM cells*.

The cells were inspected regularly for morphological alterations and for contamination by mycoplasmas. No morphological alterations of cells and no contamination by mycoplasmas could be detected.

3.3 Apparatus, glassware and small items of equipment

- CO_2 incubator, Nunc GmbH & Co. KG, model QWJ 350
- Agitator (Vortex Genie Mixer, type G 560E)
- pH measurement 315i (WTW, article no. 2A10-100)
- Centrifuge (Sigma-Aldrich-Chemie GmbH, type 113)
- Microscope (Olympus, type CK 30)
- Centrifuge 5804 R (Eppendorf AG)
- Water bath (JULABO, Julabo U 3)
- Adjustable and fixed-volume pipettes (Eppendorf AG)

4. Experimental conditions

Test temperature	20°C ± 0.5°C
Concentration of test product	3.0 % and 0.3 %
Contact times	1 and 2 minutes
Interfering substance	fetal calf serum (FCS)
Procedure to stop action of disinfectant	immediate dilution
Diluent	water of standardised hardness
Virus strain	Herpes Simplex Virus type 1
Date of testing	17.11.2008 – 08.04.2009
End of testing	08.04.2009

5. Methods

5.1 Preparation of test virus suspension

For preparation of test virus suspension, *BGM cells* were cultivated with Dulbecco´s Modified Eagle´s Medium (DMEM, Lonza Group Ltd., catalogue no. BE12-707F) and 10 % or 2 % fetal calf serum (FCS, Biochrom AG, D-12247 Berlin, Germany).
BGM cells were infected with a multiplicity of infection of 0.1. After cells showed a cytopathic effect, they were subjected to a onefold freeze/thaw procedure followed by a low speed centrifugation (10 min and 1000 x g) in order to sediment cell debris. After aliquotation, test virus suspension was stored at – 80°C.

5.2 Preparation of disinfectant (dilutions)

The test product was evaluated as 3.0 % and 0.3 % solutions. The solutions were prepared with hard water (1.25-fold of the desired concentrations) immediately before the inactivation experiments.

5.3 Inactivation assays and controls

Tests were carried out in accordance with the DVV and RKI guideline (1). Eight parts by volume of the disinfectant were mixed with one part by volume of test virus suspension and one part by volume of Aqua bidest. In tests with interfering substance, instead of Aqua bidest., one part by volume of fetal calf serum was added. Immediately at the end of the chosen exposure time, activity of the disinfectant was stopped by serial dilutions.

Due to a more convenient handling and due to a limited amount of test virus suspension, the volumes in the inactivation assay were 0.1 mL test virus suspension, 0.1 mL interfering substance and 0.8 mL test product.

Virus controls were incorporated after the longest exposure time. One part by volume of test virus suspension was mixed with nine parts by volume of Aqua bidest. or with one part by volume of FCS and eight parts by volume of Aqua bidest.

A control was carried out with one part by volume of test virus suspension, four parts by volume of PBS (0.1 M, pH value 7.0) and five parts by volume of 1.4 % formaldehyde solution. 5, 15, 30 und 60 minutes were chosen as contact times.

For determination of cytotoxicity of the disinfectant, two parts by volume of Aqua bidest. were mixed with eight parts by volume of the disinfectant, diluted with ice-cold DMEM and inoculated onto permissive cells. Values are given as $\log_{10}CD_{50}$/mL (in analogy to $\log_{10}TCID_{50}$/mL).

For the control of cell sensitivity two parts by volume Aqua bidest. or one part by volume of FCS and one part by volume Aqua bidest were mixed with eight parts by volume of the lowest apparently non-cytotoxic dilution of the product or PBS. This mixture was added to the permissive cell culture. After 1 h at 37°C the mixture was discharged and a comparative titration of the test virus suspension was performed on the pre-treated and non pre-treated (PBS) cells as described above.

Inactivation tests were carried out in sealed test tubes (Sarstedt AG & Co., D-51588 Nümbrecht, Germany) in a water bath at 20°C ± 0.5°C. Aliquots were retained after appropriate exposure times, and the residual infectivity was determined.
The inactivation experiments were run in two independent assays (two different days).

A control of efficiency for suppression of disinfectant activity was not included since at the end of the exposure time dilutions were done immediately.
Furthermore, a cell control was incorporated.

5.4 Determination of infectivity

Infectivity was determined by means of end point dilution titration in a micro-procedure. For this, samples were diluted with ice-cold DMEM with 2 % FCS and 100 µL of each dilution were placed in 8 wells of a sterile polystyrene flat bottomed microtitre plate (Nunc A/S, DK-4000 Roskilde, Denmark). 100 µL of a fresh trypsinized *BGM cells* were added. Suspension was adjusted to reach approximately 10-15 x 10^3 cells per well. Incubation was at 37°C in a CO_2-atmosphere (5.0 % CO_2 - content). Finally, cultures were observed for cytopathic effects for ten days of inoculation. The infective dose ($TCID_{50}$) (with 95 % level of confidence) was calculated according to the method of Spearman (2) and Kärber (3) with the following formula:

$$- \log_{10}TCID_{50} = X_0 + 0.5 - \sum r/n$$

meaning

X_0 = $\log_{10}$ of the lowest dilution with 100 % positive reaction

r = number of positive determinations of lowest dilution step with 100 % positive and all higher positive dilution steps

n = number of determinations for each dilution step.

5.5 Calculation and verification of virucidal activity

The virucidal activity of the test disinfectant was evaluated by calculating the decrease in titre in comparison with the control titration without disinfectant (virus control). The difference is given as reduction factor (RF).

According to the guideline (Leitlinie) of DVV/RKI, a disinfectant or a disinfectant solution at a particular concentration is having virus-inactivating efficacy if within the recommended exposure period the titre is reduced at least by four $\log_{10}$ steps.

6. Results

6.1 Determination of cytotoxicity

In parallel with the inactivation tests, the cytotoxicity of CAVEX ImpreSafe (3.0 % and 0.3 %) and 0.7 % formaldehyde was measured. The formaldehyde solution was toxic for the *BGM cells* in the 1:100 dilutions. This corresponded to a $\log_{10}CD_{50}$/mL of 3.50 (Table 1).
Examinations also showed that the disinfectant CAVEX ImpreSafe tested as 3.0 % solution achieved a $\log_{10}CD_{50}$/mL of 3.50. The 0.3 % solution was cytotoxic in the 1:10-dilutions. This corresponded to a $\log_{10}CD_{50}$/mL of 2.50 (Table 1).
These tests to measure cytotoxicity are imperative, because in this manner the lower detection threshold for non-inactivated HSV-1 could be determined.

6.2 Control of cell sensitivity

A non-cytotoxic concentration of the disinfectant might inhibit the virus replication. Therefore, the cell sensitivity in a non-cytotoxic concentration was evaluated by a comparative titration.
The comparative virus titration on cells treated with the disinfectant and PBS resulted in a difference of ≤ 0.5 $\log_{10}$ of virus titre in the presence of the disinfectant demonstrating that virus replication was not inhibited (Table 3).

6.3 Virus-inactivating properties of formaldehyde control

Results of inactivation tests are found in table 3. Formaldehyde (0.7 %) reduced the HSV-1 titre after five minutes by 2.00 ± 0.46 $\log_{10}$ steps. After 15 and 30 minutes reduction factors of

3.13 ± 0.53 and ≥ 4.25 ± 0.33 were measured. After 60 minutes the reduction of virus titre reached ≥ 4.25 ± 0.33 log_{10} steps (Table 3).

6.4 Virus-inactivating properties of disinfectant

Results of inactivation assays are demonstrated in tables 2 to 4.
The disinfectant CAVEX ImpreSafe was examined as 3.0 % and as 0.3 % solutions. 1 and 2 minutes were chosen as exposure times.

CAVEX ImpreSafe was active against HSV-1 as 3.0 % solution in all assays after one minute of exposure. The reduction factors were ≥ 4.00 ± 000 and ≥ 4.25 ± 0.33 (assays without soil load) and ≥ 4.25 ± 0.33 and ≥ 4.00 ± 0.35 (assays with FCS), respectively. The following mean values were calculated: ≥ 4.13 ± 0.16 (assays without soil load) and ≥ 4.13 ± 0.24 (assays with FCS).

The 0.3 % solution was chosen for testing the disinfectant in the non-active range. Table 4 shows that even this concentration was active in the assay with FCS within one minute. The reduction factor was ≥ 5.25 ± 0.33 at that time point.

Due to the lack of virological guidelines simulating practical conditions in Europe (phase 2, step 2 tests) the data of this quantitative suspension test lead to the recommendation to use the disinfectant CAVEX ImpreSafe for inactivation of HSV-1 as follows:

3.0 % 1 min

- Dr. J. Steinmann -

7. Quality control

The Quality Assurance of the results was maintained by performing the determination of the virus-inactivating properties of the disinfectant in accordance with Good Laboratory Practice regulations:

1) Chemicals Act of Germany, Appendix 1, dating of 01.08 1994 (BGBl. I, 1994, page 1703). Appendix revised at 14. 05. 1997 (BGBl. I, 1997, page 1060).
2) OECD Principles of Good Laboratory Practice (revised 1997); OECD Environmental Health and Safety Publications; Series on Principles of Good Laboratory Practice and Compliance Monitoring – Number 1. Environment Directorate, Organization for Economic Co-operation and Development, Paris 1998.

The plausibility of the results was additionally confirmed by controls incorporated in the inactivation assays.

8. Recorders to be maintained

All testing data, protocol, protocol modifications, the final report, and correspondence between MikroLab GmbH and the sponsor will be stored in the archives at MikroLab GmbH.

9. Literature

1. Leitlinie der Deutschen Vereinigung zur Bekämpfung der Viruskrankheiten (DVV) e.V. und des Robert Koch-Institutes (RKI) zur Prüfung von chemischen Desinfektionsmitteln auf Wirksamkeit gegen Viren in der Humanmedizin (in der Fassung vom 01.08.2008) Hyg & Med, 33, 2008, 315-322

2. Spearman, C.: The method of `right or wrong cases` (constant stimuli) without Gauss's formulae.
Brit J Psychol; 2 1908, 227-242

3. Kärber, G.: Beitrag zur kollektiven Behandlung pharmakologischer Reihenversuche.
Arch Exp Path Pharmak; 162, 1931, 480-487

Table 1: cytotoxicity of CAVEX ImpreSafe and 0.7% formaldehyde

			dilutions				
	conc.	**soil load**	**10^{-1}**	**10^{-2}**	**10^{-3}**	**10^{-4}**	**10^{-5}**
product	0.3%	Aqua bidest.	n.d.	n.d.	n.d.	n.d.	n.d.
product	0.3%	10.0% FCS	+	-	-	-	-
product	3.0%	Aqua bidest.	+	+	-	-	-
product	3.0%	10.0% FCS	+	+	-	-	-
formaldehyde	0.7%	PBS	+	+	-	-	-

Table 2 (1st assay): inactivation of HSV-1 by CAVEX ImpreSafe (3.0%) and formaldehyde (0.7%) in a quantitative suspension test at 20°C

product	conc.	soil load	$log_{10}TCID_{50}$/mL with 95% level of confidence after				reduction factor with 95% level of confidence after				≥ 4 log_{10} reduction after
			1 min	2 min	3 min	5 min	1 min	2 min	3 min	5 min	
test product	3.0%	Aqua bid.	≤3.50±0.00	≤3.50±0.00	n.d.	n.d.	≥3.75±0.33	≥3.75±0.33	n.a.	n.a.	≥ 1 min
test product	3.0%	10.0% FCS	≤3.50±0.00	≤3.50±0.00	n.d.	n.d.	≥3.88±0.25	≥3.88±0.25	n.a.	n.a.	≥ 1 min
controls	**conc.**	**soil load**	**$log_{10}TCID_{50}$/mL with 95% level of confidence after**				**reduction factor with 95% level of confidence after**				**≥ 4 log_{10} reduction after**
			5 min	**15 min**	**30 min**	**60 min**	**5 min**	**15 min**	**30 min**	**60 min**	
formaldehyde	0.7%	PBS	n.d.	n.d.	n.d.	n.d.	n.a.	n.a.	n.a.	n.a.	n.a.
virus control	n.a.	Aqua bid.	n.d	n.d.	n.d.	7.25±0.33	n.a.	n.a.	n.a.	n.a.	n.a.
virus control	n.a.	FCS	n.d.	n.d.	n.d.	7.38±0.25	n.a.	n.a.	n.a.	n.a.	n.a.
interference control PBS	n.a.	-	n.d.	n.d.	n.d.	n.d.	n.a.	n.a.	n.a.	n.a.	n.a.
interference control disinf.	n.a.	Aqua bid.	n.d.	n.d.	n.d.	n.d.	n.a.	n.a.	n.a.	n.a.	n.a.
interference control disinf.	n.a.	10.0% FCS	n.d.	n.d.	n.d.	n.d.	n.a.	n.a.	n.a.	n.a.	n.a.

n.d. = not done n. a. = not applicable

Table 3 (2nd assay): inactivation of HSV-1 by CAVEX ImpreSafe (3.0%) and formaldehyde (0.7%) in a quantitative suspension test at 20°C

product	conc.	soil load	$log_{10}TCID_{50}$/mL with 95% level of confidence after				reduction factor with 95% level of confidence after				≥ 4 log_{10} reduction after
			1 min	2 min	3 min	5 min	1 min	2 min	3 min	5 min	
test product	3.0%	Aqua bid.	≤3.50±0.00	≤3.50±0.00	n.d.	n.d.	≥4.00±0.00	≥4.00±0.00	n.a.	n.a.	1 min
test product	3.0%	10.0% FCS	≤3.50±0.00	≤3.50±0.00	n.d.	n.d.	≥4.25±0.33	≥4.25±0.33	n.a.	n.a.	1 min
controls	**conc.**	**soil load**	**log10TCID50/mL with 95% level of confidence after**				**reduction factor with 95% level of confidence after**				**≥ 4 log_{10} reduction after**
			5 min	**15 min**	**30 min**	**60 min**	**5 min**	**15 min**	**30 min**	**60 min.**	
formaldehyde	0.7%	PBS	5.75±0.33	4.63±0.41	≤3.50±0.00	≤3.50±0.00	2.00±0.46	3.13±0.53	≥4.25±0.33	≥4.25±0.33	30 min
virus control	n.a.	Aqua bid.	n.d.	n.d.	n.d.	7.50±0.00	n.a.	n.a.	n.a.	n.a.	n.a.
virus control	n.a.	FCS	n.d.	n.d.	n.d.	7.75±0.33	n.a.	n.a.	n.a.	n.a.	n.a.
interference control PBS	n.a.	-	n.d.	n.d.	n.d.	8.00±0.38	n.a.	n.a.	n.a.	n.a.	n.a.
interference control disinf.	n.a.	Aqua bid.	n.d.	n.d.	n.d.	7.75±0.33	n.a.	n.a.	n.a.	n.a.	n.a.
interference control disinf.	n.a.	10.0% FCS	n.d.	n.d.	n.d.	7.75±0.33	n.a.	n.a.	n.a.	n.a.	n.a.

n.d. = not done n. a. = not applicable

Table 4 (3rd assay): inactivation of HSV-1 by CAVEX ImpreSafe (3.0%) in a quantitative suspension test at 20°C

product	conc.	soil load	$log_{10}TCID_{50}$/mL with 95% level of confidence after				reduction factor with 95% level of confidence after				≥ 4 log_{10} reduction after
			1 min	2 min	3 min	5 min	1 min	2 min	3 min	5 min	
test product	3.0%	Aqua bid.	≤3.50±0.00	≤3.50±0.00	n.d.	n.d.	≥4.25±0.33	≥4.25±0.33	n.a.	n.a.	1 min
test product	3.0%	10.0% FCS	≤3.50±0.00	≤3.50±0.00	n.d.	n.d.	≥4.00±0.35	≥4.00±0.35	n.a.	n.a.	1 min
controls	**conc.**	**soil load**	**log10TCID50/mL with 95% level of confidence after**				**reduction factor with 95% level of confidence after**				**≥ 4 log_{10} reduction after**
			5 min	**15 min**	**30 min**	**60 min**	**5 min**	**15 min**	**30 min**	**60 min.**	
formaldehyde	0.7%	PBS	n.d.	n.d.	n.d.	n.d.	n.a.	n.a.	n.a.	n.a.	n.a.
virus control	n.a.	Aqua bid.	n.d.	n.d.	n.d.	7.75±0.33	n.a.	n.a.	n.a.	n.a.	n.a.
virus control	n.a.	FCS	n.d.	n.d.	n.d.	7.50±0.35	n.a.	n.a.	n.a.	n.a.	n.a.
interference control PBS	n.a.	-	n.d.	n.d.	n.d.	n.d.	n.a.	n.a.	n.a.	n.a.	n.a.
interference control disinf.	n.a.	Aqua bid.	n.d.	n.d.	n.d.	n.d.	n.a.	n.a.	n.a.	n.a.	n.a.
interference control disinf.	n.a.	10.0% FCS	n.d.	n.d.	n.d.	n.d.	n.a.	n.a.	n.a.	n.a.	n.a.

n.d. = not done n. a. = not applicable

Table 5: inactivation of HSV-1 by CAVEX ImpreSafe (0.3%) in a quantitative suspension test at 20°C

product	conc.	soil load	$log_{10}TCID_{50}$/mL with 95% level of confidence after				reduction factor with 95% level of confidence after				≥ 4 log_{10} reduction after
			1 min	2 min	3 min	5 min	1 min	2 min	3 min	5 min	
test product	0.3%	Aqua bid.	n.d.	n.d.	n.d.	n.d.	n.a.	n.a.	n.a.	n.a.	n.a.
test product	0.3%	10.0% FCS	≤2.50±0.00	≤2.50±0.00	n.d.	n.d.	≥5.25±0.33	≥5.25±0.33	n.a.	n.a.	1 min
controls	**conc.**	**soil load**	**$log_{10}TCID_{50}$/mL with 95% level of confidence after**				**reduction factor with 95% level of confidence after**				**≥ 4 log_{10} reduction after**
			5 min	**15 min**	**30 min**	**60 min**	**5 min**	**15 min**	**30 min**	**60 min**	
formaldehyde	0.7%	PBS	n.d.	n.d.	n.d.	n.d.	n.a.	n.a.	n.a.	n.a.	n.a.
virus control	n.a.	Aqua bid.	n.d.	n.d.	n.d.	n.d.	n.a	n.a.	n.a.	n.a.	n.a.
virus control	n.a.	FCS	n.d.	n.d.	n.d.	7.75±0.33	n.a	n.a.	n.a	n.a.	n.a
interference control PBS	n.a.	-	n.d.	n.d.	n.d.	n.d.	n.a.	n.a.	n.a.	n.a.	n.a.
interference control disinf.	n.a.	Aqua bid.	n.d.	n.d.	n.d.	n.d.	n.a.	n.a.	n.a.	n.a.	n.a.
interference control disinf.	n.a.	10.0% FCS	n.d.	n.d.	n.d.	n.d.	n.a.	n.a.	n.a.	n.a.	n.a.

n.d. = not done n. a. = not applicable

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HSV efficacy of CAVEX ImpreSafe in a quantitative suspension test at 20°C similar to the guideline of DVV/RKI dating 01.08.2008

EXPERT OPINION

This expert opinion is based on the test report O08ML710H dating 08.04.2009.

The virus-inactivating properties of the disinfectant CAVEX ImpreSafe of Cavex Holland BV against HSV were investigated by a quantitative suspension test similar to the guideline of the Deutsche Vereinigung zur Bekämpfung der Viruskrankheiten e.V. (German Association for the Control of Virus Diseases) and the Robert Koch-Institute (RKI).

According to this suspension test, a disinfectant or a disinfectant solution at a particular concentration is considered as having virus-inactivating properties if within the recommended exposure period the titre is reduced by ≥ 4 $\log_{10}$ (inactivation ≥ 99.99 %).

CAVEX ImpreSafe was examined as 3.0 % solution at 20°C. 1 and 2 minutes were chosen as exposure times. After an exposure time of one minute virus reduction exceeded 4 $\log_{10}$-steps. Therefore, a virucidal activity was measured as follows:

3.0 % **1 min**

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HSV-Wirksamkeit von CAVEX ImpreSafe im quantitativen Suspensionsversuch bei 20°C in Anlehnung an die Leitlinie von DVV/RKI in der Fassung vom 01.08.2008

GUTACHTEN

Dieses Gutachten basiert auf dem Prüfbericht O08ML710H vom 08.04.2009.

Das Desinfektionsmittel CAVEX ImpreSafe der Cavex Holland BV wurde gemäß Auftrag auf seine virusinaktivierenden Eigenschaften gegenüber dem HSV in Anlehnung an die Leitlinie der Deutschen Vereinigung zur Bekämpfung der Viruskrankheiten e.V. (DVV) und des Robert Koch-Instituts (RKI) untersucht.

Nach der Leitlinie der DVV und des RKI wird dann von einer Virus-Wirksamkeit eines Desinfektionsmittels ausgegangen, wenn nach einer bestimmten Einwirkzeit eine Reduktion des initialen Virustiters um ≥ 4 $\log_{10}$-Stufen (Inaktivierung ≥ 99,99 %) erfolgt ist.

Das Desinfektionsmittel CAVEX ImpreSafe wurde als 3,0 %ige Lösung bei 20°C untersucht. Die Einwirkzeiten betrugen 1 und 2 Minuten. Nach einer Minute war eine Reduktion des Virustiters in allen Ansätzen um ≥ 4 $\log_{10}$-Stufen nachweisbar. Somit ergibt sich eine Wirksamkeit wie folgt:

3,0 % **1 Minute**

Dr. J. Steinmann

Appendix Table 1: Raw data (HSV) of CAVEX ImpreSafe (1st assay) (1762)

product	concentration	interfering substance	exposure time (min.)	dilutions (log_{10})								
				1	2	3	4	5	6	7	8	9
product	3.0 %	Aqua bidest.	1	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	n.d.	n.d.
			2	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	n.d.	n.d.
			3	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
			5	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
		10.0% FCS	1	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	n.d.	n.d.
			2	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	n.d.	n.d.
			3	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
			5	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
product cytotoxicity	3.0 %	Aqua bidest.	n.a.	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	n.d.	n.d.	n.d.	n.d.
		10.0% FCS	n.a.	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	n.d.	n.d.	n.d.	n.d.
virus control with columns	n.a.	Aqua bidest.	n.a.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	n.a.	10.0% FCS	n.a.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
virus control without columns	n.a.	Aqua bidest.	n.a.	4444 4444	4444 4444	4444 4444	4444 4444	4444 4444	1030 4434	0000 0000	0000 0000	n.d.
	n.a.	10.0% FCS	n.a.	4444 4444	4444 4444	4444 4444	4414 4444	4444 4444	4444 2304	0000 0000	0000 0000	n.d.

n.a. = not applicable
n.d. = not done

t = cytotoxic

0 = no virus detectable
1 to 4 = virus detectable (degree of CPE in 8 wells of a microtitre plate)

Appendix Table 2: Raw data (HSV) of CAVEX ImpreSafe (2nd assay) (1787)

product	concentration	interfering substance	exposure time (min.)	dilutions (log_{10})								
				1	2	3	4	5	6	7	8	9
product	3.0 %	Aqua bidest.	1	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	n.d.	n.d.
			2	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	n.d.	n.d.
			3	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
			5	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
		10.0% FCS	1	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	n.d.	n.d.
			2	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	n.d.	n.d.
			3	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
			5	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
product cytotoxicity	3.0 %	Aqua bidest.	n.a.	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	n.d.	n.d.	n.d.	n.d.
		10.0% FCS	n.a.	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	n.d.	n.d.	n.d.	n.d.
virus control with columns	n.a.	Aqua bidest.	n.a.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	n.a.	10.0% FCS	n.a.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
virus control without columns	n.a.	Aqua bidest.	n.a.	4444 4444	4444 4444	4444 4444	4444 4444	4444 4444	4442 4444	0000 0000	0000 0000	n.d.
	n.a.	10.0% FCS	n.a.	4444 4444	4444 4444	4444 4444	4414 4444	4444 4444	3444 4444	0024 0000	0000 0000	n.d.

n.a. = not applicable
n.d. = not done

t = cytotoxic

0 = no virus detectable
1 to 4 = virus detectable (degree of CPE in 8 wells of a microtitre plate)

Appendix Table 3: Raw data (HSV) of CAVEX ImpreSafe (3rd assay) (1787)

product	concentration	interfering substance	exposure time (min.)	dilutions (log_{10})								
				1	2	3	4	5	6	7	8	9
product	3.0 %	Aqua bidest.	1	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	n.d.	n.d.
			2	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
			3	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
			5	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
		10.0% FCS	1	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	n.d.	n.d.
			2	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
			3	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
			5	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
product cytotoxicity	3.0 %	Aqua bidest.	n.a.	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	n.d.	n.d.	n.d.	n.d.
		10.0% FCS	n.a.	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	n.d.	n.d.	n.d.	n.d.
virus control with columns	n.a.	Aqua bidest.	n.a.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	n.a.	10.0% FCS	n.a.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
virus control without columns	n.a.	Aqua bidest.	n.a.	4444 4444	4444 4444	4444 4444	4444 4444	4444 4444	4444 4444	4400 0000	0000 0000	n.d.
	n.a.	10.0% FCS	n.a.	4444 4444	4444 4444	4444 4444	4414 4444	4444 4444	4440 4444	0004 0000	0000 0000	n.d.

n.a. = not applicable
n.d. = not done

t = cytotoxic

0 = no virus detectable
1 to 4 = virus detectable (degree of CPE in 8 wells of a microtitre plate)

Appendix Table 4: Raw data (HSV) of CAVEX ImpreSafe (1787)

product	concentration	interfering substance	exposure time (min.)	dilutions (log_{10})								
				1	2	3	4	5	6	7	8	9
product	0.3 %	Aqua bidest.	1	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
			2	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
			3	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
			5	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
		10.0% FCS	1	tttt tttt	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	n.d.
			2	tttt tttt	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	n.d.
			3	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
			5	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
product cytotoxicity	0.3 %	Aqua bidest.	n.a.	tttt tttt	0000 0000	0000 0000	0000 0000	0000 0000	n.d.	n.d.	n.d.	n.d.
		10.0% FCS	n.a.	tttt tttt	0000 0000	0000 0000	0000 0000	0000 0000	n.d.	n.d.	n.d.	n.d.
virus control with columns	n.a.	Aqua bidest.	n.a.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	n.a.	10.0% FCS	n.a.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
virus control without columns	n.a.	Aqua bidest.	n.a.	4444 4444	4444 4444	4444 4444	4444 4444	4444 4444	4442 4444	0000 0000	0000 0000	n.d.
	n.a.	10.0% FCS	n.a.	4444 4444	4444 4444	4444 4444	4414 4444	4444 4444	3444 4444	0024 0000	0000 0000	n.d.

n.a. = not applicable
n.d. = not done

t = cytotoxic

0 = no virus detectable
1 to 4 = virus detectable (degree of CPE in 8 wells of a microtitre plate)

Appendix Table 5: Raw data (HSV) of formaldehyde control (20°C) (1787)

product	concentration	interfering substance	exposure time (min)	dilutions (log_{10})								
				1	2	3	4	5	6	7	8	9
formaldehyde	0.7% (m/V)	PBS	5	tttt tttt	tttt tttt	4433 2444	2112 3212	0002 0010	0000 0000	0000 0000	0000 0000	n.d.
			15	tttt tttt	tttt tttt	1112 2220	1001 0000	0000 0000	0000 0000	0000 0000	0000 0000	n.d.
			30	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	n.d.
			60	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	0000 0000	n.d.
formaldehyde cytotoxicity	0.7% (m/V)	PBS	n.a.	tttt tttt	tttt tttt	0000 0000	0000 0000	0000 0000	n.d.	n.d.	n.d.	n.d.

n.a. = not applicable
n.d. = not done

t = cytotoxic

0 = no virus detectable
1 to 4 = virus detectable (degree of CPE in 8 wells of a microtitre plate)

Appendix Table 6: raw data for cell sensitivity (1787)

product	interfering substance	dilutions	dilutions (log_{10})								
			1	2	3	4	5	6	7	8	9
PBS	-	n.a.	4444 4444	4444 4444	4444 4444	4444 4444	4444 4444	4444 4444	0004 0444	0000 0000	n.d.
product	Aqua bidest.	1:10	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
		1:100	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
		1:1,000	4444 4444	4444 4444	4444 4444	4444 4444	4444 4444	4444 4444	0400 0040	0000 0000	n.d.
product	FCS	1:10	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
		1:100	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
		1:1,000	4444 4444	4444 4444	4444 4444	4444 4444	4444 4444	4444 4444	0040 4000	0000 0000	n.d.

n.a. = not applicable
n.d. = not done

t = cytotoxic

0 = no virus detectable
1 to 4 = detection of virus (degree of CPE in 8 wells of a microtitre plate)