

Methods for the Evaluation of Hand Disinfectants

Dr. Manfred Rotter, University of Vienna, Austria

Sponsored by Deb Hand Hygiene www.deb.co.uk

Methods for the Evaluation of Hand Disinfectants



Manfred L. Rotter

Institute of Hygiene and Medical Microbiology
Medical University of Vienna

Hosted by Paul Webber
paul@webbertraining.com
www.webbertraining.com

Sponsored by

Experts in Cleaning & Hygiene
www.deb.co.uk

Rotter/teleclass/2005/Bo

1

Evaluation of Hand Disinfectants (1) Parameter: Reduction of bioburden

➤ *In vitro*

- MIC of disinfectant vs. selected strains
- MBC of disinfectant vs. selected strains
- Quantitative suspension tests for (bacteri-, fungi-, viru-)cidal properties
- Kill-time studies suspension tests

Rotter/teleclass/2005/Bo

2

Evaluation of Hand Disinfectants (2)

➤ *In vivo*

- Controlled laboratory tests simulating practical conditions on hands of volunteers
- Field trials

Rotter/teleclass/2005/Bo

3

Evaluation of Hand Disinfectants (3) Parameter: Reduction of infections

➤ Clinical trial

- Comparative trial with the aim
⇒ Novum > Reference
- Equivalence study

Rotter/teleclass/2005/Bo

4

SAMPLE SIZE NECESSARY FOR SIGNIFICANT DIFFERENCE OF PROPORTIONS (Example for comparative trial)

PRESENT RATIO OF HAND-TRANSMITTED NOSOCOMIAL INFECTIONS p_1	2 %
Desired reduction of infection ratio p_2	50 %
NEW RATIO OF HAND-TRANSMITTED NOSOCOMIAL INFECTIONS intended p_2	1 %
Level of significance (one-sided)	$\alpha = 5 %$
Power of statistical test	$1 - \beta = 90 %$
SAMPLE SIZE (= Number patients per experimental arm)	2500

Rotter/teleclass/2005

5

Laboratory Test Methods

Hygienic Hand Disinfection:
(Hygienic Hand *Wash* and Hygienic Hand *Rub*)

In vitro

In vivo

A Webber Training Teleclass

Hosted by Paul Webber paul@webbertraining.com

www.webbertraining.com

Page 1

Methods for the Evaluation of Hand Disinfectants

Dr. Manfred Rotter, University of Vienna, Austria

Sponsored by Deb Hand Hygiene www.deb.co.uk

Bactericidal Properties of Hand Disinfectants Proposed Suspension test prEN 12054

In vitro

Test organisms

Staphylococcus aureus
Pseudomonas aeruginosa
Escherichia coli K 12
Enterococcus hirae

Temperature

20°C

Contact time

- hygienic

1 min (optional 0,5 min)

- surgical

5 min (optional 1,2,3,4 min)

Requirement

reduction: rub 5.0 lg,
wash 3.0 lg

Rotter/teleclass/2005/Bo

7

HYGIENIC HANDRUB/HANDWASH

REFERENCE ONE HALF OF VOLUNTEERS

UNDER TEST OTHER HALF OF VOLUNTEERS

CONTAMINATION
E. COLI MOTO
100%
AIR DRY (2min)

PRE-DISINFECTION
SAMPLING (1min)

DISINFECTION

POST-DISINFECTION
SAMPLING (1min)

In 2nd test: same volunteers
perform test with changed roles

Rotter/teleclass/2005/Bo

8

Hygienic Handwash with antiseptic soap – EN 1499. Simulating practical Conditions

In vivo

Volunteers

12-15

Test organism

Escherichia coli K 12

Recovery

Fingertip rub before and after treatment

Application

- product

30 or 60 s, according to manufacturer

- reference

60 s handwash with unmedicated soap

Requirement

Product significantly ($p = 0.01$ unidirectional)
more efficacious than soap

Discrimination

Means ≥ 0.5 lg different (Power: 0.90)

Rotter/teleclass/2005/Bo

9

Hygienic Handrub – EN 1500 Simulating practical Conditions

In vivo

Volunteers

12-15

Test organism

Escherichia coli K 12

Recovery

Fingertip rub before and after treatment

Application:

- product

30 or 60 s, according to manufacturer

- reference

2 x 30s (=60 s) handrub with 2x3 ml

60% (vol) 2-propanol

Requirement

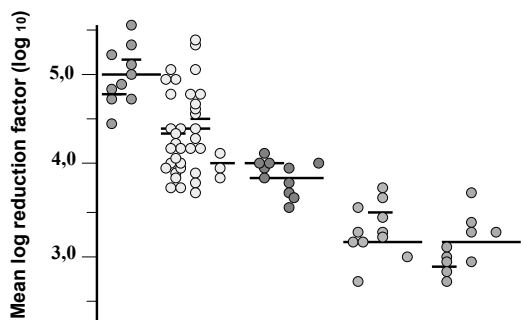
Product not significantly ($p = 0.1$, unidir.)
less efficacious than 2-propanol 60%, 1min

Discrimination

Means ≥ 0.6 lg different (Power: 0.95)

Rotter/CHCA/Deinf_03
Rotter/teleclass/2005/Bo

10



Place ...
Preparation: n-Propanol 50%
Iso-Propanol 60% Standard
Ethanol 70% + chlorhex. 0,5%
Povidone-I-0,75% soap
Phenolic soap

Hygienic Hand Disinfection – ANOVA: non-standardized Results (lg RF_{Pj}): 5 agents, 5 repetitions, 2 laboratories, with 15 volunteers in each

Source of Variation	DF	Mean Squares	F	P
Agents (5)	4	102,4	327,5	<0,0001
Volunteers (15)	14	2,6	8,1	<0,0001
Laboratories (2)	1	5,8	18,6	<0,0001
PxV	42	0,7	2,2	<0,0001
VxL	3	3,4	10,8	<0,0001
PxL	14	3,1	10,0	<0,0001
PxVxL	42	0,7	2,4	<0,0001
Error	470	0,3		

Rotter/WB0/2004/Bo

12

A Webber Training Teleclass

Hosted by Paul Webber paul@webbertraining.com

www.webbertraining.com

Page 2

Methods for the Evaluation of Hand Disinfectants

Dr. Manfred Rotter, University of Vienna, Austria

Sponsored by Deb Hand Hygiene www.deb.co.uk

Hygienic Hand Disinfection – ANOVA:
standardized results (lg RF_{Pre}-lg RF_{Post}):
4 [products–reference], 5 repetitions, 2 laboratories,
with 15 volunteers in each

Source of Variation	DF	Mean SQ	F	P
Products-Reference (4)	3	90,2	117,5	<0,00001
Volunteers (15)	14	2,7	3,5	<0,00001
Laboratories (2)	1	3,5	4,6	n.s.
PxV	42	0,9	1,1	n.s.
VxL	3	1,6	2,1	n.s.
PxL	14	1,7	2,1	<0,01
PxVxL	42	0,9	1,2	n.s.
Error	466	0,8		

Rotter/WHO 2004/Bo 13

Health-Care Antiseptic Drug Products-FDA (1)

In vitro

- **Antibacterial spectrum** of
 - active ingredient
 - carrier
 - both
- **MICs** with 20 microbial species, 50 strains of each (50% fresh clinical strains)
 - 9 gramnegative spp.
 - 10 grampositive spp.
 - Candida (incl. C. albicans) (= approx. 1000 strains)
- **Development of resistance study**
- **Time-kill study** (suspension test) with selected strains for 0, 3, 6, 9, 12, 15, 20, 30 min

Rotter/teleclass/2005/Bo 14

Health-Care Antiseptic Drug Products - FDA (2)
Antiseptic handwash and Health-Care Personnel handwash (originally ASTM E 1174)

In vivo

- **Volunteers (N):** approx. total of 108
 - Test preparation: approx. 54
 - Positive control: approx. 54
- **Contaminant bacterium:** *Serratia marcescens*, (*E. coli*)
- **Contamination and application:** 10 times on an experimental day (Test and control in parallel)
- **Samplings:**
 - after 1st contamination (baseline)
 - after 1st, 3rd, 7th, 10th wash (rub)
- **Required reduction within 5min:**
 - after 1st handwash: 2 lg
 - after 10th handwash: 3 lg

Rotter/teleclass/2005/Bo 15

Standard Test Method for Determining the Bacteria Reducing Effectiveness of Hygienic Handwash and Handrub. ASTM E 2276

In vivo
(Similar to “Virus-eliminating“ Test acc. to ASTM E-1838)

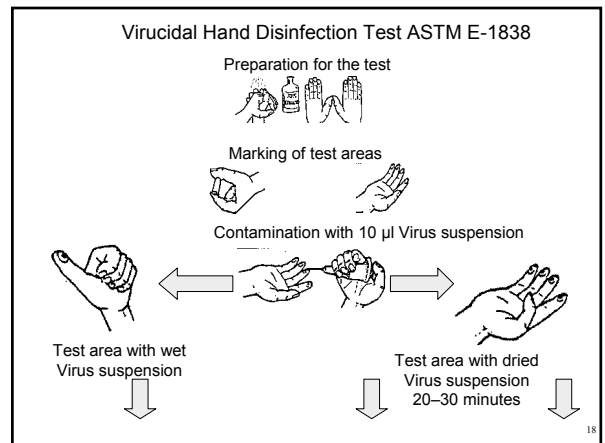
Finger Pads including thumbs of at least 2 volunteers
Test bacteria: *S. marcescens*, *E. coli*, *S. aureus*, *S.epiderm.*
Requirement: not defined, but in comparison to a negative and positive control

16

Virucidal Hand Disinfection Tests

Suspension Tests		In vivo Tests	
		Finger pad	Whole hand
<u>prEN 14476</u>	<u>DVV</u>	<u>ASTM E-1838</u> (acc. to Sattar)	<u>ASTM E-2011</u> (Steinmann)
Polio 1	Polio 1	Adeno (human 4)	Rota (human)
Adeno 5	Adeno	Rota (human) Wa	Rhino (human)
	Vaccinia	Rhino (human) 37	Rhino (human)
	SV 40	Hepatitis A HM-175	
4.0 lg	4.0 lg	not defined	not defined

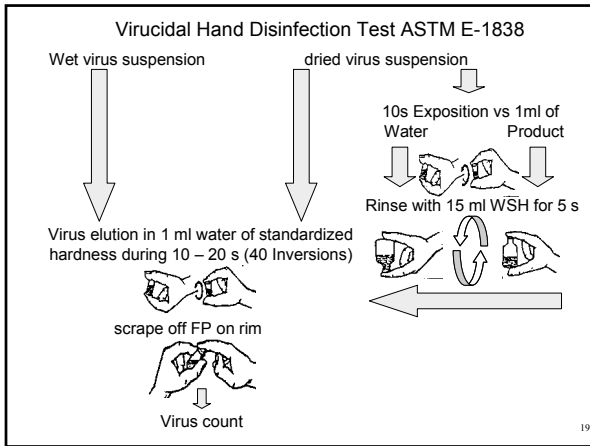
17



Methods for the Evaluation of Hand Disinfectants

Dr. Manfred Rotter, University of Vienna, Austria

Sponsored by Deb Hand Hygiene www.deb.co.uk



Laboratory Test Methods

Surgical Hand Disinfection:
(Surgical Hand *Wash* and Surgical Hand *Rub*)

In vitro
In vivo

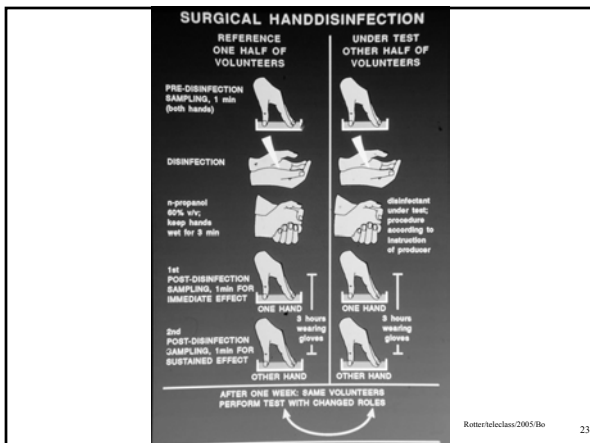
Laboratory Test Methods

Surgical Hand Disinfection:
In vitro

Same Test Method as for Hygienic Hand Disinfection

Laboratory Test Methods

Surgical Hand Disinfection:
In vivo



Surgical Handrub/wash – prEN 12791
Simulating practical conditions

In vivo

Volunteers (N): 18-20

Test organism: Resident skin flora

Recovery: Fingertip rub before and after treatment

Application of

- Product: acc. to manufacturer, max.5 min handrub/wash
- Reference: 3 min handrub with 60%/vol 1-propanol (nx3 ml)

Immediate effect sample: immediately after end of treatment (one hand)

3-hours effect sample: 3 hrs after end of treatment (other [gloved] hand)

Requirement: Product not significantly (imm: p=0.1; 3-hrs: 2p =0.01) less efficacious than reference

Discrimination: imm. Effect: Means ≥ 0.5 lg different (Power: 0.95)

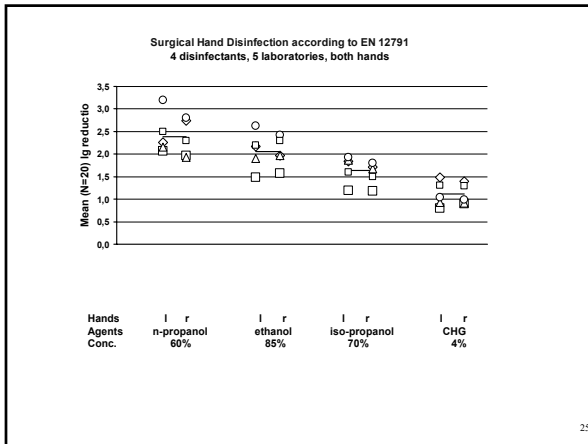
Sustained effect: Optional claim: At 3 hrs, product significantly (p=0.01, unidirectional) more efficacious than reference

Rotter/teleclass/2005/Bo/2003 24

Methods for the Evaluation of Hand Disinfectants

Dr. Manfred Rotter, University of Vienna, Austria

Sponsored by Deb Hand Hygiene www.deb.co.uk



Surgical Hand Disinfection - ANOVA :
non-standardized results (lgRF_i);
4 agents , 2 hands, 5 laboratories, 20 volunteers in each

Source of Variation	DF	F	p
1 Agents (4)	3	53,97	< 0,001 *
2 Laboratories (5)	4	5,22	< 0,001 *
3 Hands (2)	1	4,93	0,029
1 x 2	12	1,67	0,073
1 x 3	4	1,37	0,249
2 x 3	3	0,66	0,579
1 x 2 x 3	12	1,55	0,107

Rotter/WHO 2004/Bo2003

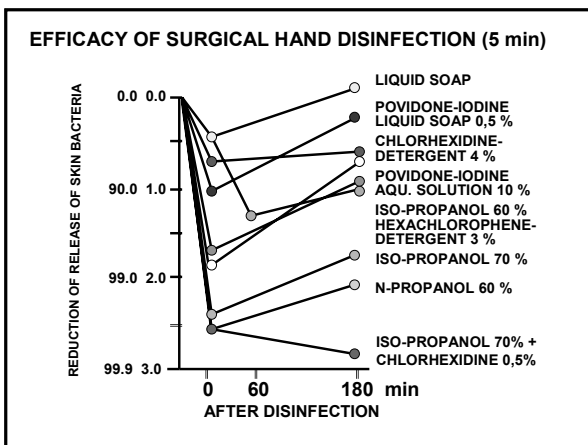
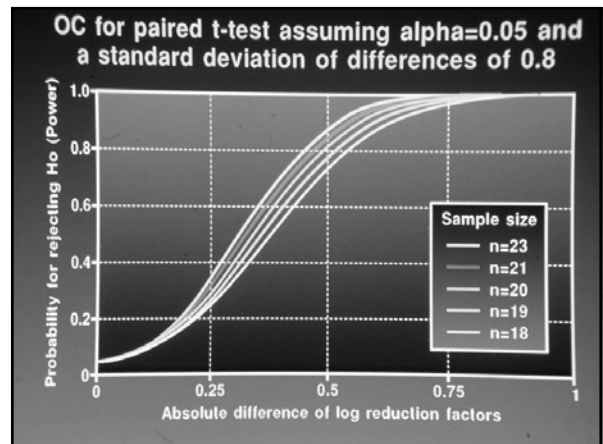
26

Surgical Hand Disinfection - ANOVA :
standardized results (lgRF_{Pi} - lgRF_{Ri});
3 [products -reference], 5 laboratories, 2 hands,
20 volunteers in each

Source of Variation	DF	F	p
1 [Products-Reference] (3)	2	42,16	< 0,001 *
2 Laboratories (5)	4	1,67	0,162
3 Hands (2)	1	0,70	0,404
1 x 2	8	1,66	0,109
1 x 3	4	3,41	0,012
2 x 3	2	0,63	0,533
1 x 2 x 3	8	0,40	0,918

Rotter/WHO 2004/Bo2003

27



Surgical Hand Disinfection: FDA (orig. ASTM E 1115)

Volunteers (N): approx: 100 (150)
per arm:

- Test: approx. 50
- Positive control: approx. 50
- (Placebo) (50)

Testbacteria: normal resident handflora

Application of Product:
acc. to manufacturer's instruction or
without any: apply product 2 x 5 min, then
rinse hands for 1 min

„Baseline“:
rinse hands for 30 s, wash hands for 30s,
rinse hands for 30s

Positive control: FDA-approved antiseptic; all parameters
as product; concurrent testing

48 mg Rotter/bocklass2005

30

Methods for the Evaluation of Hand Disinfectants

Dr. Manfred Rotter, University of Vienna, Austria

Sponsored by Deb Hand Hygiene www.deb.co.uk

Surgical Hand Disinfection: FDA *in-vivo* model
Schedule for disinfecting and sampling and required
lg bacterial reduction

Sampling Times (hrs)	Day of test periode				
	1	2	3	4	5
1/60	lg	⊗	x	x	⊗
3	O	⊗	x	x	O
6	<bl	⊗g	x	x	⊗g

X: Desinfection: Day 1 (1/60), day 2, 3, 4 (1/60, 3, 6), day 5 (1/60)

O: Sampling: Day 1, 2 and 5: after 1/60, 3 and 6 hrs with gloves

bl: Baseline

Rotter/teleclass/2005

31

Thank You for Your Attention

Further Information is available!

Other 2005 Teleclasses

For more information, refer to
www.webbertraining.com/schedule.cfm

- April 21 – Creutzfeldt-Jakob Disease: Recommendations for Disinfection and Sterilization with Dr. William Rutala
- April 28 – Overcoming the Resistance of Biofilms with Dr. Peter Gilbert
Sponsored by Virox Technologies Inc. www.virox.com
- May 19 – Antiseptic Practice & Procedure with Susan Crow
Sponsored by 3M Canada www.3m.ca
- May 26 – Canadian Response to West Nile Virus with Dr. Paul Sockett
- June 7 – Measuring the Cost of Hospital Infection with Dr. Barry Cookson

Questions? Contact Paul Webber paul@webbertraining.com

33

A Webber Training Teleclass

Hosted by Paul Webber paul@webbertraining.com

www.webbertraining.com