Evaluation of virucidal efficacy of alcohol-based hand rubs against norovirus – comparison of international test methods

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INTRODUCTION

The virucidal efficacy of alcohol-based hand rubs (ABHRs) is essential for ensuring infection prevention. While in Europe virucidal claims are accepted, the FDA does not allow such claims for ABHRs. The virucidal efficacy of ABHRs can be tested with *in-vivo* methods including the whole hand method ASTM E2011-13 or EN 1500.

OBJECTIVES

We studied the activity of a commercial ABHR and 70 % ethanol as reference against the clinically relevant norovirus. For this purpose the murine norovirus (MNV) was utilized as a surrogate. The main objective of the study was to increase the scientific and regulatory acceptance for evaluating the virucidal efficacy of ABHRs.

METHODS

For efficacy evaluation a commercially available ABHR (80 % w/w ethanol) was utilized. 70 % w/w ethanol served as a reference solution and was included in the study as well. The murine norovirus strain S99 served as test virus. Activity tests were performed *in-vivo* according to ASTM E2011-13 (five subjects in each group) and additionally in a cross-over design based on EN 1500 (19 subjects).

Table 1: Comparison of both test methods, ASTM E2011-13 and EN 1500, for virucidal efficacy evaluation of alcohol-based hand rubs (modified according to Jacobshagen et. al)*

	ASTM E2011-13	EN1500 (now prEN 17430:2019)
Evaluation handrub possible	Yes	Yes
Evaluation hand wash possible	Yes	No
Test viruses	Different viruses possible	Only MNV
Contamination procedure	Whole hand	Finger pad
Cross-over design	No, results from different volunteers are compared	Yes
Reference	No internal reference	70 % w/w ethanol
Calculation of reduction in virus infectivity	For handwash: Comparison of log_{10} reduction between hands after application of test substance and post-treatment water-rinse with application of hard water only. For handrub: Comparison between hands treated with test substance and hands treated with salt solution (EBSS) or other medium control.	Reduction factors are calculated from individual log pre and log post values after treatment with either reference or test product.
Pass criteria	No prescribed statistical evaluation method or other pass criteria.	The mean reduction with the test product shall be at least not inferior to that achieved by the reference (70 % w/w ethanol)
Independent from contributing factors like differences between subjects, application etc.	No	Yes
Confirmation by Ethics committee in Europe possible	No	Yes

RESULTS

Table 2: ABHR efficacy test according to EN 1500 (prEN 17430:2019) with MNV as test virus. Shown are the log_{10} reduction factors (RF)

Test person	Reference solution	Commercial preparation	Test person	Reference solution	Commercial preparation
1	2.88	2.56	11	2.13	2.69
2	3.06	3.56	12	4.00	4.13
3	2.94	3.13	13	2.00	2.56
4	2.00	3.06	14	4.19	3.94
5	3.00	2.94	15	4.19	4.19
6	1.94	2.69	16	2.44	2.37
7	3.31	3.25	17	2.63	2.38
8	1.00	0.69	18	1.88	1.44
9	1.81	1.94	19	3.88	4.06
10	2.81	3.06	Mean value log RF	2.74	2.88

Table 3: ABHR efficacy test according to ASTM E2011-13 with MNV as test virus

	Baseline	Reference solution					Commercial preparation				
Test person	A	B	C	D	E	F	G	H	I	J	K
log_{10} $TCID_{50}$/ml	6.00	≤ 1.50	2.25	2.25	2.00	1.75	1.75	1.75	≤ 1.50	2.00	1.75
Average log_{10} $TCID_{50}$/ml		1.95					1.75				
RF [log_{10}]		≥ 4.50	3.75	3.75	4.00	4.25	4.25	4.25	≥ 4.50	4.00	4.25
Average RF [log_{10}]		4.05					4.25				
Average % reduction		≥ 99.99 %					≥ 99.99 %				

Based on EN 1500 70 % w/w ethanol and the tested ABHR showed comparable mean log reductions (RF) of 2.74 and 2.88, respectively. According to ASTM E2011-13 the RF was 4.05 for 70 % w/w ethanol and 4.25 for the tested ABHR. No statistical difference was measured between the test preparations ($p > 0.05$).

CONCLUSION

+ Methodological factors like contamination, way of application and recovery might result in different RFs of both methods.
+ However, the methods are able to yield similar results when comparing with the ethanol reference.
+ The EN 1500 suggests a cross-over design with a mandatory control group.
+ This results in an activity evaluation, which is independent from contributing factors including differences between subjects, application etc.
+ The ASTM E2011-13 additionally allows comparing disinfecting with mechanical effect.
+ A combination of both methods might be considered to get an internationally accepted method for virucidal efficacy evaluation of ABHRs.