Technoleg Iechyd Cymru
Health Technology Wales

Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

1. Determine the quantity and quality of evidence available for a technology of interest.
2. Identify any gaps in the evidence/ongoing evidence collection.
3. Inform decisions on topics that warrant fuller assessment by Health Technology Wales.

Topic:	Does the use of hydrogen peroxide vapour to reprocess single-use personal protective equipment devices result in safe levels of residual hydrogen peroxide?
Topic exploration report number:	TER206

Introduction and aims

Guidance issued by Public Health bodies recommends that filtering facepiece respirators, disposable aprons and disposable fluid-repellent coveralls or long-sleeved gowns should be worn by health professionals to offer protection against COVID-19 (Public Health England. 2020).

While disposable personal protective equipment (PPE), such as filtering facepiece respirators (respirators) and isolation/surgical gowns, are not approved for routine decontamination as standard of care, PPE decontamination and reuse may be needed during times of shortage to ensure continued availability during the COVID-19 pandemic.

Hydrogen peroxide vapour (HP vapour) could be used as a method to decontaminate PPE. An effective decontamination method should reduce the pathogen burden, maintain the function of the PPE, but also present no residual chemical hazard. The Health and Safety Executive Workplace Exposure Limits for use with the Control of Substances Hazardous to Health Regulations states that the long-term (eight-hour time-weighted average reference period) workplace exposure limit of hydrogen peroxide is one part per million (ppm) (1.4 milligrams per cubic metre), and the short-term (15-minute reference period) workplace exposure limit of hydrogen peroxide is 2 ppm (2.8 milligrams per cubic metre) (Health and Safety Executive. 2020).

Health Technology Wales researchers searched for evidence that reported levels of residual hydrogen peroxide (HP) after use of HP vapour to decontaminate PPE, in particular respirators and isolation/surgical gowns.

Summary of evidence

Secondary Evidence

Guidance

In March and April 2020, the U.S. Food and Drug Administration (FDA) issued Emergency Use Authorisations (EUAs) for a number of systems using HP vapour to decontaminate N95 or N95-equivalent respirators (that are not cellulose based, due to the fact that cellulose absorbs HP) for reuse by healthcare workers in hospital settings during the COVID-19 pandemic. These are summarised in the Brief Literature Results section.

Part of the EUA report for the Sterilucent HC 80TT HP steriliser states that dissipation studies confirmed that residual HP on the compatible N95 respirators was reduced to safe levels (less than 1 ppm) after six-hours aeration (FDA, EUA. 2020).

Systematic reviews

We identified one preprint manuscript of a systematic review investigating the efficacy and safety of methods for decontamination of N95 and SN95 respirators. Thirteen articles were included in the systematic review. The decontamination methods included in the review were: HP vapour, liquid HP, sodium hypochlorite, ethanol, isopropyl alcohol and ethylene oxide. The systematic review stated that residual levels of liquid HP and HP vapour were reported in one and two studies, respectively, though they remained within established safety limits, and in the case of HP vapour decreased over time. The author suggested that a "holding period" following decontamination, where respirators sit for a one-week period following exposure to HP vapour, would provide extra assurance that HP levels were under the permissible exposure limit (O'Hearn et al. 2020).

A systematic review protocol studying the efficacy and safety of disinfectants for the decontamination of filtering facepiece respirators is due to be published in April 2020 [CRD42020177679]. We also identified a protocol for a second systematic review protocol (planned publication date unknown). The objective of the systematic review is to evaluate interventions, including HP vapour, used to decontaminate surgical mask PPE for the purposes of reuse (Zorko et al. 2020). It is currently unclear whether these systematic reviews will investigate residual HP levels on the PPE.

Primary evidence

One study was identified that measured the amount of residual oxidant on six models of N95 respirator using different decontamination methods, including HP vapour decontamination with the STERRAD 100S system. The study reported that all decontamination methods, other than ethylene oxide treatment, did not deposit significant quantities of toxic residues on the respirators. HP vapour left an average of 0.35 mg to 1.23 mg of oxidant on the respirators (depending on respirator type). The S1, S2, P1 and P2 models treated with HP vapour retained approximately three times as much oxidant as the other two models (Table 1). This study also noted that residual oxidant concentrated in the filter media of all of the particulate respirators but only in the filtration medium of S1 for the surgical respirators. The author concluded that the filtering media comprises the largest portion of the respirator and thus poses the greatest risk of exposure (Salter et al. 2010).

Table 1. Average amount of oxidant remaining on respirators following decontamination with HP vapour peroxide and off-gassing for 18 hours

N95 Respirator type	Average amount of oxidant remaining (mg) (95% CI)
S1 cup-shaped	1.23 (0.68 to 1.77)
S2 flat-fold	0.43 (0.29 to 0.57)
S3 duck-bill surgical FFR	0.36 (-0.11 to 0.83)
P1 cup-shaped N95 particulate FFR	1.09 (0.64 to 1.53)
P2 cup-shaped	0.81 (0.29 to 1.34)
P3 cup-shaped	0.35 (0.04 to 0.66)
CI: confidence interval; FFR: filtering facepiece respirator; mg: milligram	

In a report prepared by the organisation Battelle, five N95 respirators were exposed to a single HP vapour decontamination cycle (Bioquell system). The off-gassing from the respirator was measured three, four, and five hours into the aeration phase using a HP monitor. A total of five hours was required to achieve a non-detect for HP. HP readings taken from the masks at the tested time points are shown in Table 2. Even after only three hours of aeration, the HP concentration was below the permissible exposure limit of 1 ppm (Battelle. 2016).

Table 2. Aeration-phase HP Readings from Whole N95 FFRs

	Aeration phase duration (hours)		
	3	4	5
N95 HP concentration (ppm)	0.2	0.2	0.0
HP: hydrogen peroxide; ppm: parts per million			

One study was identified that evaluated residual HP following disinfection of N95 respirators by ionized HP (SteraMist Binary Ionization Technology solution delivered through a SteraMist Surface Unit). The level of HP on the inner surface of the respirator at two hours was 0.6 ppm and undetectable at three hours. The author suggested that the speed of HP release from N95 respirators may be variable and affected by the air current (Cheng et al. 2020).

We identified a manuscript with forthcoming publication to Applied Biosafety. A Bioquell Clarus C system was used to contaminate approximately one-hundred 3M 1860 N95 respirators. A PortaSens II sensor was used to detect HP levels over a four-hour timeframe, taking readings at regular intervals by placing the probe close to the respirators. At approximately four hours, the HP residue-levels decreased below the PortaSens II level of detection (0 ppm). In the qualitative test, three individuals did a smell test to determine if there were any noticeable odours: none were detected (Schwartz et al. 2020).

One study was identified investigating residual HP on polypropylene. Whilst the study did not specifically involve PPE, polypropylene is a commonly used material for disposable respirators and surgical/isolation gowns. The study did not use HP vapour but instead used an aqueous solution of HP to decontaminate polypropylene and other materials. They reported that polypropylene and cotton had the lowest residual concentrations of HP: the average released residual concentration was less than 0.4 micrograms/cm^2 and less than 0.1 micrograms/cm^2, respectively. The study measured the concentrations of disinfectant agents released by the

test materials, rather than the concentrations of agents adhering to them (Lerones et al. 2004).

We identified one study investigating the cytotoxicity of various medical materials decontaminated with HP vapour. After HP vapour decontamination and two hours aeration, six materials (polystyrene, polyurethane, blend material of silicone and polyurethane, poly[methyl methacrylate], fluorosilicone acrylate and poly[B hydroxyethyl methacrylate]) produced strong cytotoxicity and three materials (polypropylene, silicone and polyethylene) did not. The six materials that produced strong cytotoxicity had a 0% absorbance of control after two hours aeration, and the polypropylene had an 85% absorbance of control (standard deviation: ±7). The cytotoxicity was caused by residual HP left in the materials (Ikarashi et al. 1995).

We identified a further four studies that reported that significant levels of residual HP from respirator materials following HP vapour decontamination are unlikely and not of concern because the vapours decompose readily (Otter et al. 2007, Viscusi et al. 2007 and 2009, and McEvoy and Rowan 2019).

Cost

We identified one review that noted that the HP vapour equipment and process costs a similar amount to other gaseous modalities, such as ethylene oxide and steam sterilisation (McEvoy and Rowan. 2019). A U.S. study reported that HP vapour and ethylene oxide sterilisers are relatively expensive technologies, but that organisations that own these devices would experience only a small burden of added operational costs (Salter et al. 2010).

A randomised, prospective UK study was identified comparing the clinical and cost effectiveness of eight disinfection methods for hospital rooms contaminated with *C. difficile*, including use of HP vapour (Bioquell Q10). A cost-effectiveness analysis was undertaken comparing all disinfection methods to the method of 1,000 ppm chlorine-releasing agent (Actichlor Plus). HP vapour had a higher incremental benefit (-28.94 variance in colony count) than the chlorine-releasing agent but was £138.57 more expensive. Of the eight decontamination methods, HP vapour was ranked seventh most expensive, with a cost per use of £108.96 and a cost per month of £1,154.98 (Doan et al 2012).

Areas of uncertainty

We found limited evidence on residual HP following HP vapour decontamination of respirators, and no evidence following decontamination of surgical/isolation gowns. The only evidence we identified that could be used for surgical/isolation gowns is the study investigating aqueous solution HP decontamination of polypropylene (Lerones et al. 2004) and the study investigating cytotoxicity of polypropylene following HP vapour decontamination (Ikarashi et al. 1995). We did not identify evidence on the safety of residual HP on PPE. Further research into HP residue on PPE, particularly surgical/isolation gowns, is needed.

Whilst we identified one study comparing residual HP in the room following use of two HP decontamination systems, HP vapour versus aerosolised HP (Fu et al. 2012: summarised in the Brief Literature Results section) we did not identify any similar head-to-head comparisons of HP delivery methods and residual HP on PPE. We also did not identify any studies comparing HP residue from HP vapour systems: the Bioquell and Battelle systems are centralised systems, whereas the Steris and STERRAD systems are localised to Sterile Services Departments.

Conclusions

Respirators and surgical/isolation gowns are labelled as ‘single-use’ devices and have not been approved for reuse. Consequently, very few data are available that describe the effects on PPE following treatment with decontamination agents. The FDA published EUAs for N95 or N95-equivalent respirators (that are not cellulose based) during the COVID-19 pandemic, and note that dissipation studies confirmed that residual HP on the respirators was reduced to safe levels (less than 1 ppm) after six-hours aeration. Other evidence we identified also suggests that residual HP levels on respirators following decontamination with HP vapour are safe. We identified limited evidence for residual HP on respirators and polypropylene, and we did not identify any evidence for residual HP on other types of PPE.

Brief literature search results

Resource	Results
HTA organisations	
Healthcare Improvement Scotland	We did not identify any relevant evidence from this source
Health Technology Assessment Group	Safety Alert: Decontaminating with hydrogen peroxide (HP) technology within the HSE. Dec 2019: https://www.hse.ie/eng/staff/safetywellbeing/healthsafetyand%20wellbeing/safetyalerts.html Health Service Executive Code of Practice for Decontamination of Reusable Invasive Medical Devices: https://www.hse.ie/eng/about/who/qid/quality-and-patient-safety-documents/deccont-rimd.html
Health Information and Quality Authority	We did not identify any relevant evidence from this source
UK guidelines and guidance	
SIGN	We did not identify any relevant evidence from this source
NICE	We did not identify any relevant evidence from this source
PHE	COVID-19 PPE. April 2020: https://www.gov.uk/government/publications/wuhan-novel-coronavirus-infection-prevention-and-control/covid-19-personal-protective-equipment-ppe#section-10
HSE	EH40/2005 Workplace exposure limits: Containing the list of workplace exposure limits for use with the Control of Substances Hazardous to Health Regulations 2002: https://www.hse.gov.uk/pubns/books/eh40.htm

International guidelines and guidance	
FDA	Emergency Use Authorizations (EUAs): https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations *EUAs issued for: Sterilucent, Inc. Sterilization System; Stryker STERIZONE VP4 N95 Respirator Decontamination Cycle; Advanced Sterilization Products (ASP) STERRAD Sterilization System; STERIS Sterilization Systems for Decontamination of N95 Respirators; and Battelle Decontamination System.*
Secondary literature and economic evaluations	
ECRI	N95 Masks: New Guidance for Addressing Shortages (2020): https://www.ecri.org/landing-covid-19-medical-devices-respirator-masks/ Safety of extended use and reuse of N95 respirators. 2020: https://assets.ecri.org/PDF/COVID-19-Resource-Center/COVID-19-Clinical-Care/COVID-ECRI-N95-Respirators-updated-4.pdf
EUnetHTA	We did not identify any relevant evidence from this source
Cochrane library	We did not identify any relevant evidence from this source
Medline (Ovid)	We did not identify any relevant evidence from this source
Other (contacted author from a study on PROSPERO)	Preprint Manuscript: O'Hearn k; Gertsman S; Webster R; Tsampalieros A; Ng R; Gibson J; Sampson M; Sikora L; and McNally JD. 2020. Efficacy and Safety of Disinfectants for Decontamination of N95 and SN95 Filtering Facepiece Respirators: A Systematic Review https://osf.io/ct6m8/
Primary studies	
Cochrane library	We did not identify any relevant evidence from this source
Medline	Cheng V, Wong SC, Kwan G, Hui WT, Yuen KY. 2020. Disinfection of N95 respirators by ionized hydrogen peroxide in pandemic coronavirus disease 2019 (COVID-19) due to SARS-CoV-2. Journal of Hospital Infection https://doi.org/10.1016/j.jhin.2020.04.003 Doan L, Forrest H, Fakis A, Craig J, Claxton L, Khare M. Clinical and cost effectiveness of eight disinfection methods for terminal disinfection of hospital isolation rooms contaminated with Clostridium difficile 027. 2012. Journal of Hospital Infection, 82: 114-121 https://doi.org/10.1016/j.jhin.2012.06.014 Fu TY, Kumar GV. 2012. Efficacy, efficiency and safety aspects of hydrogen peroxide vapour and aerosolized hydrogen peroxide room disinfection systems. Journal of Hospital Infection, 80: 199-205

https://doi.org/10.1016/j.jhin.2011.11.019

Head-to-head comparison of HP vapour (Clarus R, Bioquell) and aerosolized hydrogen peroxide (SR2, Sterinis, now supplied as Glosair, Advanced Sterilization Products (ASP), Johnson & Johnson Medical Ltd, room disinfection systems. Two hours after the start of the cycles, the mean concentration of hydrogen peroxide in the room 1.3 (standard deviation [SD] 0.4) ppm and 2.8 (SD 0.8) ppm for the four HP vapour and aHP cycles, respectively. This indicates that the room was not safe to enter at the manufacturer's recommended time after the Sterinis cycles.

Ikarashi Y, Tsuchiya T, Nakamura A. 1995. Cytotoxicity of medical materials sterilized with vapour-phase hydrogen peroxide. Biomaterials 16(3): 177-183
https://doi.org/10.1016/0142-9612(95)92115-M

Lerones C, Marisacal M, Carnero A, Garcia-Rodriguez, Fernandez-Crehuet J. 2004. Clin Microbiol Infect, 10: 984–989
https://doi.org/10.1111/j.1469-0691.2004.00967.x

McEvoy B and Rowan NJ. 2019. Terminal sterilization of medical devices using vaporized hydrogen peroxide: a review of current methods and emerging opportunities. Journal of Applied Microbiology 127: 1403-142
https://doi.org/10.1111/jam.14412

Otter JA, Cummins M, Ahmad F, van Tonder C, Drabu YJ. 2007. Assessing the biological efficacy and rate of recontamination following hydrogen peroxide vapour decontamination. Journal of Hospital Infection, 67(2): 182–188:
https://doi.org/10.1016/j.jhin.2007.07.019

Salter WB, Kinney K, Wallace WH, Lumley AE, Heimbuch BK, Wander JD. 2010. Analysis of Residual Chemicals on Filtering Facepiece Respirators After Decontamination. Journal of Occupational and Environmental Hygiene, 7:8, 437-445
https://doi.org/10.1080/15459624.2010.484794

Schwartz A, Stiegel M, Greeson N, Vogel A, Thomann W, Brown M, Sempowski GD, Alderman TS, Condreay JP, Burch J, Wolfe C, Smith B, Lewis S.
Decontamination and Reuse of N95 Respirators with Hydrogen Peroxide Vapor to Address Worldwide Personal Protective Equipment Shortages During the SARS-CoV-2 (COVID-19) Pandemic. Manuscript accepted for publication in Applied Biosafety. Publication forthcoming.
https://www.lackawannacounty.org/wp-content/uploads/2020/03/N-95_VHP-Decon-Re-Use.pdf

Viscusi DJ, King WP, Shaffer RE. 2007. Effect of Decontamination on the Filtration Efficiency of Two Filtering Facepiece Respirator Models. Journal of the International Society for Respiratory Protection, 24: 93-107
https://www.isrp.com/the-isrp-journal/journal-public-abstracts/1138-vol-24-no-3-and-no-4-2007-pp-93-107-viscusi-open-access/file

Viscusi DJ, Bergman MS, Eimer BC, Shaffer RE. 2009. Evaluation of Five Decontamination Methods for Filtering Facepiece Respirators. The Annals of Occupational Hygiene, 53(8): 15–827

	https://doi.org/10.1093/annhyg/mep070
Ongoing primary or secondary research	
PROSPERO database	Efficacy of different methods of disinfection and sterilization to reuse masks and respirators: a systematic review and meta-analysis [CRD42020177679]. Review ongoing. Anticipated completion date: 30 April 2020: https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=177679 Manuscript due to be published in the near future: Zorko DJ, Choong K., McNally D, O'Hearn K, Sampson M, & Sikora L. 2020. Decontamination interventions for the reuse of surgical mask personal protective equipment (PPE): A protocol for a systematic review: https://doi.org/10.31219/osf.io/8wt37
Clinicaltrials.gov	We did not identify any relevant evidence from this source
Other	
Google	Battelle. Final Report for Bioquell HP Vapour Decontamination for Reuse of N95 Respirators. 2016: https://www.fda.gov/media/136386/download

Date of search:	April 2020
Concepts used:	Hydrogen peroxide, residual, residue, off-gas, exposure level, HPV, VHP, HP system, Bioquell, Batelle, Steris, Sterrad, H2O2, decontamination, decontaminate, reprocess, re-process, single-use, personal protective equipment, PPE, respirator, face mask, N95, FFP2, FFP3, gown, polypropylene, cotton, cost