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HOT AIR DECONTAMINATION LANDSCAPE SURVEY

Summary Report, version 1.0

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The Johns Hopkins University Applied Physics Laboratory

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Interim Report**

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EXECUTIVE SUMMARY

Emerging and re-emerging pathogens are a considerable threat to global health security and are a leading global health concern. The infectious diseases caused by these pathogens are of direct concern and have considerable impact on military personnel and safety due to potential spread events from the surrounding areas, or within military communities during operations and deployments. Outbreaks of infectious diseases within a military installation may require direct treatment or patient transport to a secondary location. To enable effective patient transport when infectious disease transmission and control is a risk, the United States Air Force (USAF) needs rapid and reliable patient transport aircraft disinfection procedures to maintain readiness of essential personnel and transport aircraft. The USAF also needs to identify knowledge and procedural gaps involving infection control in patient transport that require further research and improvement.

Current methods for disinfecting transport aircraft after patient transport follow hot air decontamination protocols that require dedicated, specialized equipment with significant set up and temperature adjustment times. These procedures can be time consuming and have not been optimized toward specific organism disinfection. Investigations of feasible alternate decontamination protocols are necessary to balance minimized disinfection time and maximized effectiveness for return to duty.

The USAF, via Air Force Research Laboratory (AFRL), seeks standardization of decontamination protocols to be implemented on or within aircraft to mitigate transmission of infectious diseases or pathogenic organisms. Of particular interest is aircraft decontamination after patient transport. To aid in this effort, the Johns Hopkins University Applied Physics Laboratory (JHU/APL), in support of AFRL, has completed a landscape survey investigating biological decontamination methods implemented on aircraft and non-aircraft settings. This hot air directed search is intended to provide information to aid in building a downstream predictive decontamination model for emerging pathogens.

The landscape survey identified data gaps in the limited variety of organisms tested, incomplete log reduction validation, and variation of material types. Wet lab experiments are recommended to fill these data gaps, followed by further multivariate data analysis on a more complete data picture. Investments in continued research and developing more robust data sets are essential for accurate predictive models to inform military operations.

By gathering datapoints across multiple factors such as temperature, humidity, time to decontamination, and the extent of decontamination, models can be built to predict the outcomes of these variables. While these models are undefined here, the data sets consolidated from this research provide the baseline decontamination needs for each organism or organism class. Future utility for the compiled data includes application development for mobile or computer accessibility, where novice users can interrogate data to generate decontamination processes for response to real world incidents and use.

1. INTRODUCTION

The USAF, via AFRL seeks standardization of decontamination protocols to be implemented on or within aircraft to mitigate transmission of infectious diseases or pathogenic organisms. To help achieve this goal, JHU/APL completed an initial (Phase 1) landscape survey for biological decontamination methods used on aircrafts. The report was submitted to AFRL, February 2023 as Aircraft Decontamination Landscape Survey (AOS-23-0230) and identified various methods used for decontamination of microorganisms on aircraft, including hot air as an effective method. As a next step, AFRL requested an additional, Phase 2 landscape survey exploring the use of hot air as the primary decontamination technology against biological microorganisms, agnostic to setting. In order to expand the initial study to include supplementary data specific to hot air decontamination, this follow up landscape survey was performed focusing on hot air decontamination of biological agents outside of the aircraft setting. This hot air directed search is intended to provide information to aid in building a downstream predictive decontamination model for emerging pathogens. Future utility for the compiled data includes application development for mobile or computer accessibility, where novice users can interrogate data to generate decontamination processes for response to real world incidents and use.

To complete the Phase 2 landscape survey, JHU/APL has performed a systematic literature review incorporating specific search parameters from relevant literature databases. As the literature was identified and consolidated, survey parameter information such as operational setting, aircraft relevant materials, and organisms tested was extracted, recorded, and consolidated into an excel database.

This report summarizes the process followed for conducting a landscape survey and describes the overall format of the consolidated landscape survey database. The associated landscape survey database is in the form of a standalone excel spreadsheet that will be submitted along with this report. Extracted data is presented, specifically highlighting decontamination parameters for hot air decontamination methods, organisms evaluated for decontamination, and time to decontamination.

2. METHODS, ASSUMPTIONS, AND PROCEDURES

To execute a large-scale landscape survey, a systematic literature review process was implemented and outlined (Appendix A). As defined in the review process (Appendix A), specified literature search-engines [Embase, Defense Technical Information Center (DTIC)] were interrogated to consolidate relevant literature. Embase, a propriety database from the vendor Elsevier, was searched instead of PubMed, because MEDLINE constitutes about 85% of PubMed, and Embase contains MEDLINE documents plus potentially relevant papers (e.g., from European journals) not in PubMed/MEDLINE. Embase also has a proprietary keyword indexing system, Emtree, which is more nuanced and easily searchable than PubMed. Appendix B details the Embase search terms and combinations used.

In the initial review stage, following selection of these research databases, data fields and terms were implemented and defined for database searches (Appendix A). Citation data and abstracts compiled from these databases were then uploaded to an online tool, Covidence, which allows for an organized, streamlined systematic review. The initial citation and abstract upload into Covidence were screened for duplicate entries, which were removed. Then remaining entries' titles plus abstracts (where abstracts were available) were screened by the JHU/APL technical team for relevance. In instances where abstracts were not available, attempts were made to retrieve the full document PDF to screen for relevance. On occasion, abstracts were present in the document PDF but not viewable in Covidence, because issues with metadata quality precluded the abstract text from being imported into Covidence. All title/abstracts deemed relevant, per the outlined project parameters (Appendix A), were then moved to full text review. For the 705 title/abstracts deemed relevant, full text PDFs were sought for retrieval.

In the full text review stage, team members assessed documents and their contents against predetermined inclusion/exclusion criteria (Appendix A). As with the title/abstract screening in the prior stage, two team members conducted full text review independently, with conflicts over whether to include or exclude, resolved by a third team member. Having multiple reviewers aids in minimizing screening bias and supports a more robust data acquisition process. Documents falling under exclusion criteria ($n = 595$) were tagged with their reason for exclusion in Covidence (see Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart in Figure 1 for exclusion detail). Documents marked for inclusion ($n = 110$), proceeded to the data abstraction stage.

Although the Covidence software contains a data abstraction module, JHU/APL chose not to use it for data abstraction, because Covidence is a cloud service not approved for all unclassified information. While the metadata for DTIC documents (author name(s), date, title, abstract) was imported in Covidence for title/abstract screening along with metadata from research database articles, when sources indicated certain DTIC papers were not approved for public release, their full text was not imported into Covidence. Instead, an established method for redaction was employed using a JHU/APL Box drive URL for the restricted document. Source documents were referenced in the “Notes” of the Covidence entry. This enabled team members to retrieve the corresponding full text PDF from JHU/APL’s Box drive, which is FedRAMP authorized, and redacted extracted data was input in Microsoft Excel.

Thus, the team used Microsoft Excel software for data consolidation, where data elements of interest make up the spreadsheet fields. Structured data choices are presented as dropdown options in Excel fields to facilitate evidence synthesis and enable filtering for specific areas of interest. These data fields included, for example: decontamination methods, organisms tested, organism type, setting and protocol verification. The complete list of column data regarding the Data Extraction Fields are found in the list below (Table 1).

Table 1 - Data Extraction Fields

| Metric | Specific Characteristics Captured |
|--|---|
| Primary Decontamination Method | Dry Heat or Humidity |
| Primary Decontamination Time | Range from ≤ 5 minutes to ≥ 24 hours |
| Primary Decontamination Method Specifics | Percent relative humidity (RH) or decontamination temperature |
| Other Decontamination Method Specifics | Percent RH or decontamination temperature if used in tandem |
| Decontamination Verification | e.g., live culture, Polymerase Chain Reaction (PCR) |
| Decontamination Efficiency | Log reduction or positive or negative subculture if log reduction not tested |
| Organism Type | Gram-negative (-) bacteria, Gram-positive (+) bacteria, spore forming bacteria, Fungus, Parasite, double-stranded Deoxyribonucleic Acid (dsDNA) virus, single-stranded Ribonucleic Acid ssRNA) (positive/negative-sense (+/-)) virus, bacteriophage |
| Organism Starting Concentration | e.g., cells/mL, TCID ₅₀ |
| Organism | Organism name with strain in parentheses if applicable |
| Setting | e.g., laboratory, laboratory coupon, vehicle, aircraft interior |
| Material | e.g., Personal Protective Equipment (PPE), stainless steel, cotton, plastic |
| Environment | e.g., laboratory, outdoor |
| Laboratory amenable | Feasibility for work be performed at JHU/APL |
| Notes | Relevant details not captured in database |
| Title | Title of Publication |
| Year | Year of Publication |
| Reviewer Initials | JHU/APL Reviewer of Publication |

3. RESULTS AND DISCUSSION

Following the methods and procedures detailed above, JHU/APL completed a landscape survey to assess hot air decontamination methods, agnostic to setting, following the process as summarized in Figure 1 below.

The PRISMA flow chart details the numbers of articles initially imported for screening (6201), 15 of which were duplicates and removed, of the 6186 abstracts screened, 705 (5479 out of 6186 were identified as irrelevant) were moved to full text review. During full text review, 110 papers were deemed to meet inclusion criteria for data extraction. These 110 texts are within the consolidated database and are summarized in the following discussion.

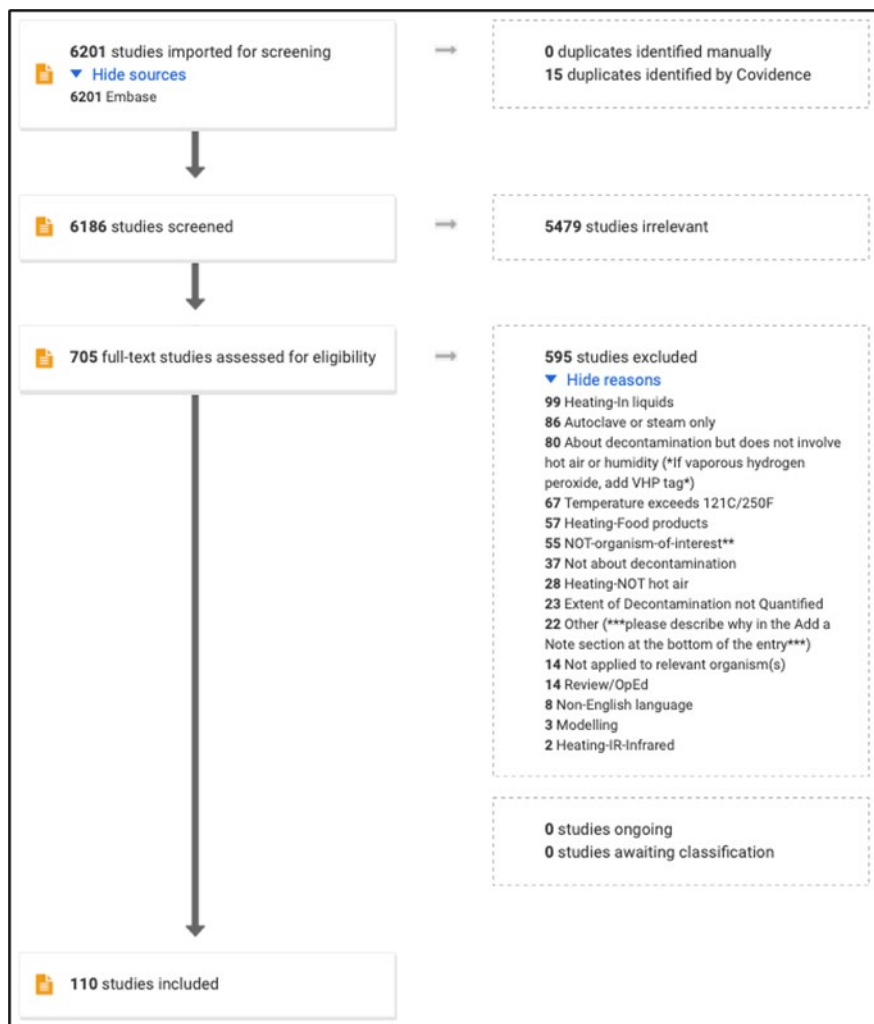


Figure 1 - Covidence PRISMA Flow Chart

3.1 Landscape Survey Decontamination Method Survey

As a result of extraction from 110 unique pieces of literature, JHU/APL recorded 1479 total data points related to decontamination by hot air (dry heat) and/or hot air with humidity. For each of the decontamination methods, detailed conclusions were made for organisms tested along with “Decontamination Efficiency” based on sample log-reduction.

3.2 Landscape Survey Results: Organism Class

A wide variety of pathogens were identified in the hot air decontamination landscape survey. As stated previously, data extraction included classifying the organism used in each paper by organism type. Organism type included Gram(+) spore-forming bacteria, Gram(+) vegetative bacteria, Gram(-) bacteria, ssRNA (+) viruses, ssRNA (-) viruses, dsDNA viruses, dsDNA viruses, ssDNA viruses, fungi, and bacteriophages. Figure 2 details the variety of organism classes captured in data extraction. Overall, Gram-positive bacteria (including both spore-forming and vegetative organisms) were the largest group of pathogens evaluated for hot air decontamination, and dsRNA viruses were the smallest group.

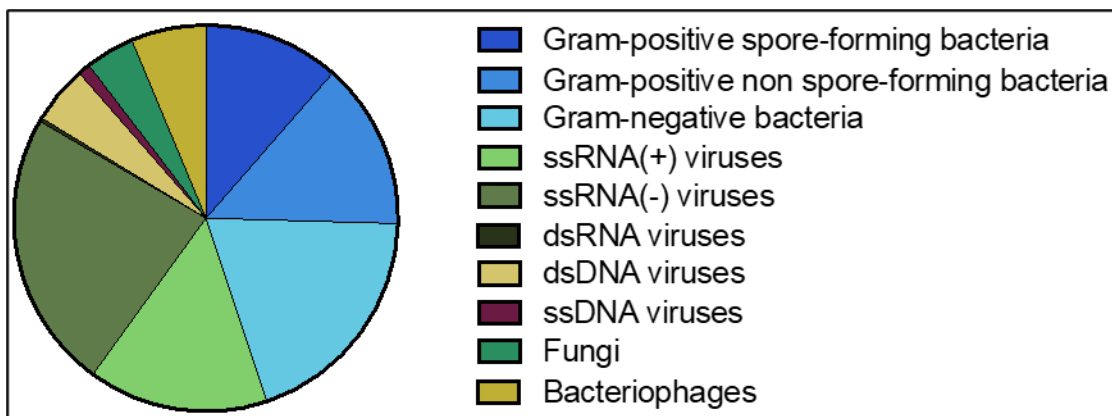


Figure 2 - Representation of the variety of organism classes identified in hot air decontamination landscape survey

Through the data extraction process, the complete organism’s name was annotated in addition to organism class. Figure 3 shows the top 18 most referenced pathogens from data extraction. Each data point represents a unique piece of literature examining hot air decontamination of the organism. The top 18 referenced pathogens include an organism from each of the class types listed above. The most referenced pathogen was *Escherichia coli* (*E. coli*), followed by *Bacillus subtilis* spores, *Staphylococcus aureus* (*S. aureus*), and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

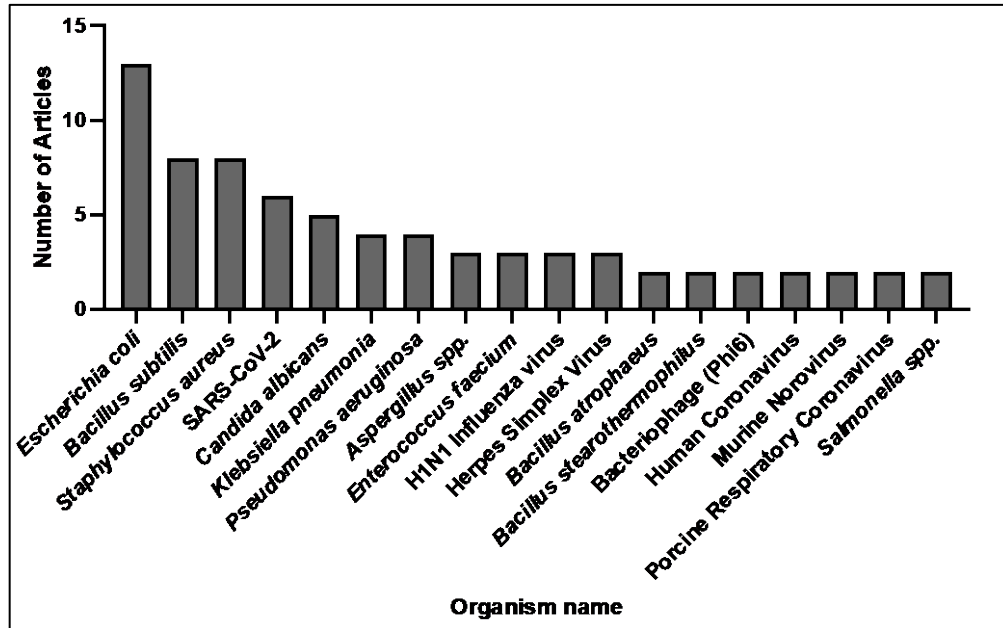


Figure 3 - Top 18 referenced pathogens

E. coli and *S. aureus* are both causative agents of common nosocomial infections and are frequently researched for novel decontamination procedures due to the rise of antibiotic resistance within both species. Spores are generally more difficult to decontaminate and require higher temperatures and decontamination times compared to vegetative cells. *Bacillus subtilis* spores are common simulants used in place of higher risk group pathogens that require a higher biosafety level (BSL) for manipulations. SARS-CoV-2 research has remained a high priority since the COVID-19 pandemic and will likely continue to be a top referenced pathogen of interest regarding communicable disease research.

All pathogens identified in the hot air decontamination landscape survey are referenced in Table 2, categorized by organism class.

Table 2 - List of pathogens identified in the hot air decontamination landscape survey

| Bacteria | | |
|--|--|--|
| Gram(-) vegetative | Gram(+) spores/spore formers | Gram(+) vegetative |
| <i>Acinetobacter baumannii</i> | <i>Bacillus spp. (anthracis ΔSterne, atropheus, canaveralius, cereus, horneckiae, nealsonii, oceanisediminis, pumilus, stearothermophilus, subtilis, subtilis var. niger, thuringiensis)</i> | <i>Corynebacterium pseudo-diphtheriae</i> |
| <i>Citrobacter freundii</i> | <i>Clostridioides difficile</i> | <i>Enterococcus faecium</i> |
| <i>Enterobacter cloacae</i> | <i>Clostridium tetani</i> | <i>Mycobacterium terrae,</i> <i>Mycobacterium tuberculosis</i> |
| <i>Escherichia coli</i> | | <i>Staphylococcus aureus,</i> Methicillin-resistant <i>Staphylococcus aureus,</i> <i>Staphylococcus saprophyticus</i> |
| <i>Klebsiella spp., Klebsiella pneumoniae</i> | | <i>Streptococcus faecalis</i> |
| <i>Salmonella spp., Salmonella typhi</i> | | |
| Virus | | |
| ssRNA (-) | ssRNA (+) | dsRNA |
| H1N1 Influenza virus | Bovine viral diarrhea virus | Human Rotavirus |
| H6N2 Influenza virus | Human Coronavirus | |
| H9N2 Influenza virus | Murine Coronavirus | dsDNA |
| Mumps virus | Murine Hepatitis virus | Adenovirus |
| | Murine Norovirus | Herpes Simplex Virus |
| Bacteriophages | Poliovirus | Polyomavirus |
| Bacteriophage (Phi6) | Porcine epidemic diarrhea virus | Vaccinia virus |
| MS2 bacteriophage | Porcine reproductive and respiratory syndrome virus | |
| | Porcine Respiratory Coronavirus | ssDNA |
| | Severe acute respiratory syndrome coronavirus 2 | Bovine parvovirus |
| | Yellow Fever virus | |
| Fungi | | |
| <i>Aspergillus spp., Aspergillus niger, Aspergillus versicolor</i> | <i>Candida albicans</i> | <i>Cladosporium cladosporioides</i> |
| <i>Microsporidian spores</i> | <i>Penicillium</i> | |

3.3 Landscape Survey Results: Decontamination Parameters and Log Reduction

All articles accepted for full-text review were evaluated for decontamination parameters and log reduction, as well as experimental setting and environment. Decontamination parameters included time to decontamination, decontamination temperature, and percent RH when applicable.

3.3.1 Decontamination Time

Significant variation was observed for the “Time to Decontamination” category within the extracted data with the majority of information collected falling under two hours. Papers with decontamination time solely greater than 48 hours were excluded from data extraction, as the timing was out of the bounds of relevance for this survey. Figure 4 shows the decontamination times across all articles, summarized into five different decontamination times less than or equal to: 30 minutes, 2 hours, 12 hours, 24 hours, or greater than 24 hours.

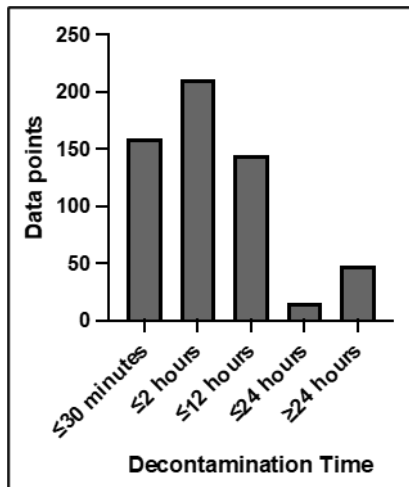


Figure 4 - Time to decontamination across all organism classes

3.3.2 Decontamination Temperature: Bacteria

Decontamination temperature and RH values varied greatly among the data collected. Numerous combinations of temperature and RHs were tested across all papers, where no conclusions could be drawn looking at the data across all organism types. Trends are evident for data evaluations exclusively within organism class or type, and specifically when focusing on bacteria derived data. Figure 5 compares decontamination temperatures for all gram(+) organisms, separating gram(+) spores from non-spore forming vegetative bacteria. More instances of higher temperature (100 degrees Celsius (°C)) required for decontamination are noted for gram(+) spore forming bacteria as opposed to gram(+) vegetative bacteria. The large majority of vegetative gram-positive studies included decontamination temperatures around 70°C.

Results displayed in Figure 6 are shown comparing all gram(+) bacteria (spore formers and non-spore formers) against gram(-) bacteria. The peaks seen at 70°C and >100°C for gram(+) bacteria are consistent with the dominate data peaks in Figure 5. For gram-negative bacteria, the referenced articles' decontamination parameters averaged 90°C, trending higher specifically from 60-90°C. Considering gram(-) bacteria are more resistant to chemical disinfectants and antibiotics than gram-positive (1), gram(-) bacteria trending toward higher temperature required for decontamination is logical from an overarching decontamination perspective.

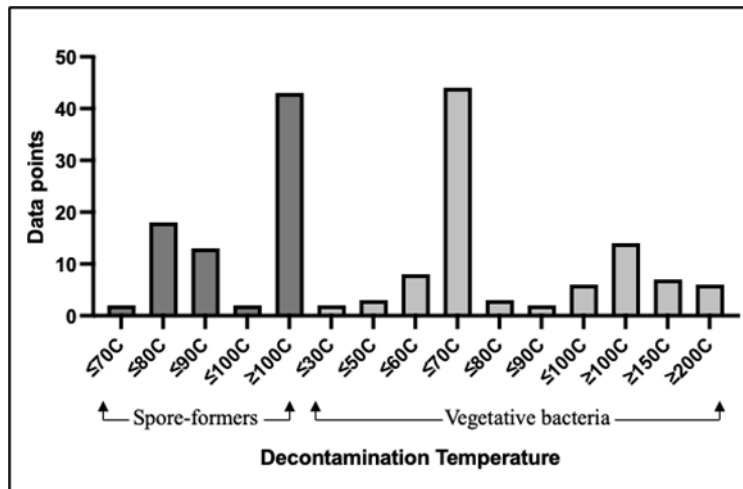


Figure 5 - Comparison between decontamination temperatures of gram(+) spore-forming and gram(-) vegetative organisms via hot air decontamination

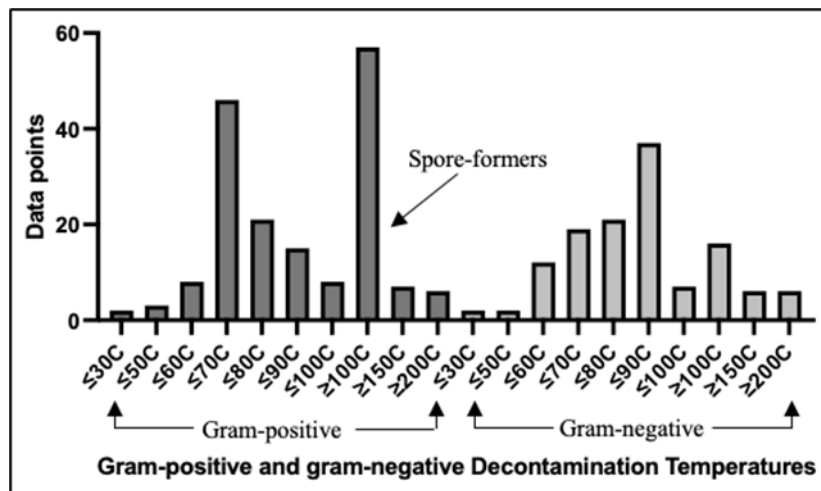


Figure 6 - Comparison of decontamination temperatures for gram(+) and gram(-) bacteria

3.3.3 Decontamination Temperature: Virus

When investigating decontamination temperature as directly related to virus, data was separated by virus genome class. As such, Figure 7 encompasses multiple graphs showing the distribution of decontamination temperatures evaluated for ssRNA (+), ssRNA (-), dsDNA, ssDNA and dsRNA viruses. As a whole, decontamination data points for ssRNA (+) viruses are more widely distributed across temperature tested, with 70°C as the temperature with the highest data peak. SARS-CoV-2 is included in this data set and is the virus most referenced in the landscape data set and accounts for most of the datapoints in the ssRNA (+) graph. Considering, inactivation of coronavirus family cultures at temperatures above 56°C has been well documented, with shorter incubation times required as temperature increases (2), hot air decontamination evaluations in this temperature range is expected.

The data displayed for the ssRNA (-) organisms shows close to 50 data entries for each of the temperatures, 30, 40, and 50°C. A closer look at the data revealed these were datapoints extracted from one article investigating survivability of avian influenza virus at various temperatures and RH. This data as related to log reduction of the virus called out when discussing data depicted in Figure 7 below. The remaining virus genome classes (dsDNA, ssDNA and dsRNA) yield less than 10 data points for each temperature category, with no distinct data represented for any one class of virus. Rotavirus and adenovirus are examples of human pathogenic viruses in these classes. As such, more in depth hot air decontamination data specific to these and all relevant infectious viruses would be important to inform parameters implemented toward hot air decontamination procedures or disinfection model and application development.

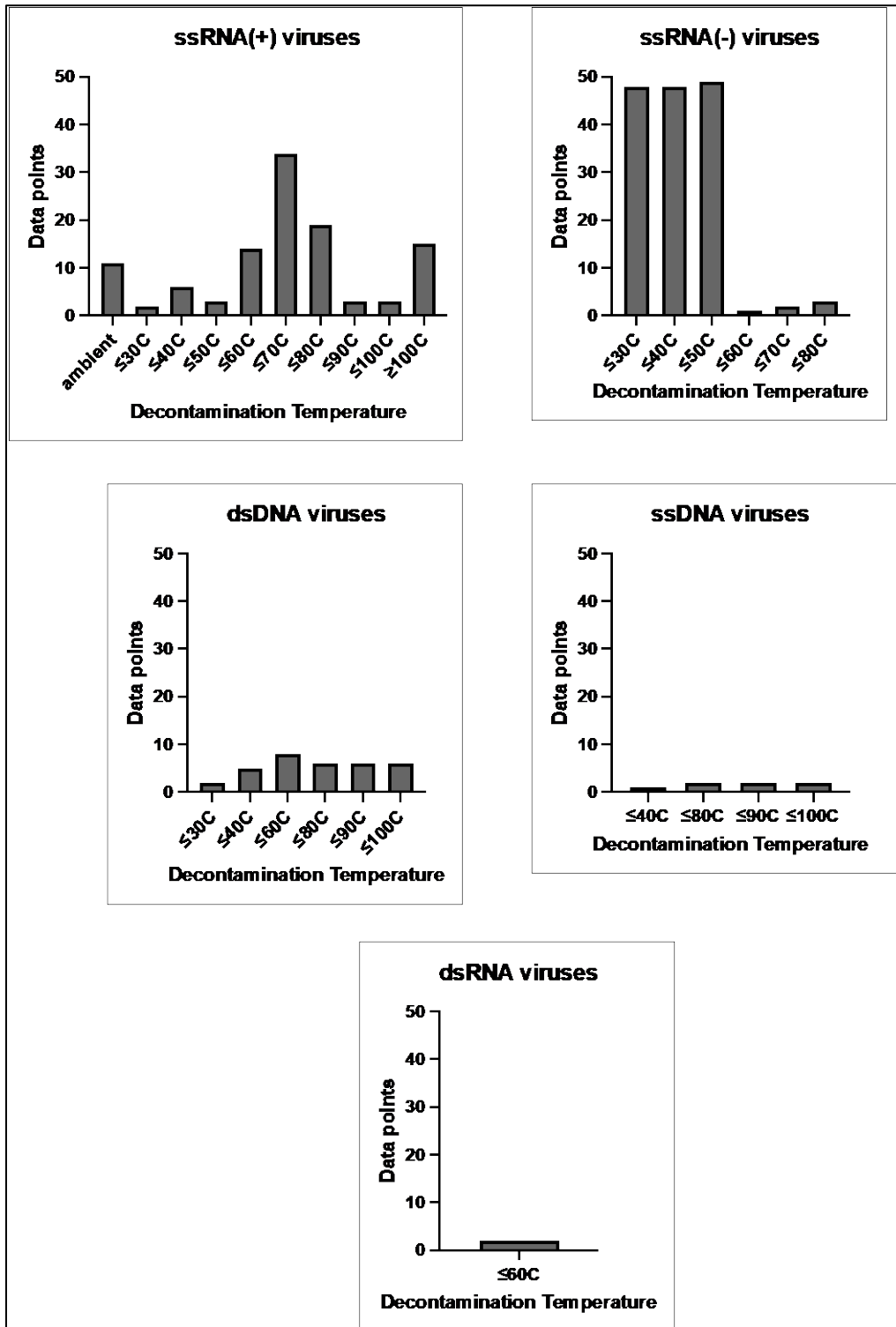


Figure 7 - Comparison of decontamination temperatures between various genome classes of viruses captured in landscape survey

3.3.4 Decontamination Temperature: Bacteriophage

Bacteriophages, often truncated to “phage”, are types of viruses that infect bacteria and while they are not infectious to humans, were included in data extraction for this landscape survey as an infectious virus simulant. Researchers will conduct experiments at a lower BSL, or biosafety level, with phage and correlate the data to genetically or structurally similar infectious virus. Over half of the datapoints extracted specific to phage decontamination were derived from a single reference and are summarized in Figure 8. This particular research article examined the effects of varying RH at temperatures 72°C ($\leq 80^{\circ}\text{C}$) and 82°C ($\leq 90^{\circ}\text{C}$) for two phages. Greater than 6 log reduction of the phage concentrations was accomplished when RH was 50% or greater. Experiments conducted at $\leq 30^{\circ}\text{C}$ were evaluating survivability of aerosolized phage particles at room temperature.

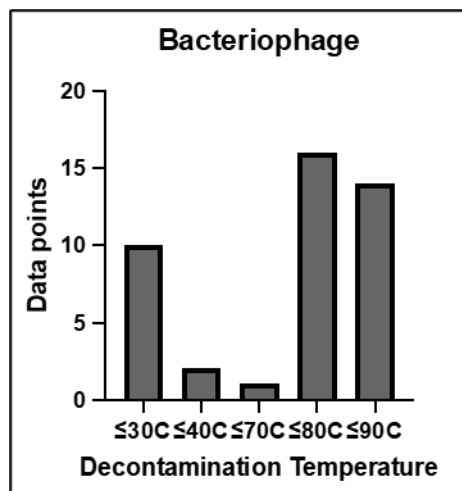


Figure 8 - Comparison of decontamination temperatures of bacteriophages

3.3.5 Decontamination Temperature: Fungi

Figure 9 represents data points consolidated from literature detailing hot air and RH decontamination events specific to fungi. Of particular interest for data captured in the $\leq 60^{\circ}\text{C}$ temperature range, was one article that looked at hot air decontamination of a bus due to fungal contaminants associated with adverse health effects to bus drivers. Hot air treatment did not exceed 60°C as to prevent “the melting of sealants, tar products, and other agents that could produce volatile gases and vapors that would defeat the purpose of the heat treatment” (3) and is noted here for potential correlations and relevance to aircraft decontamination protocols, specifically. For this particular temperature, decontamination results for the fungi varied only demonstrating complete kill for one type of fungus.

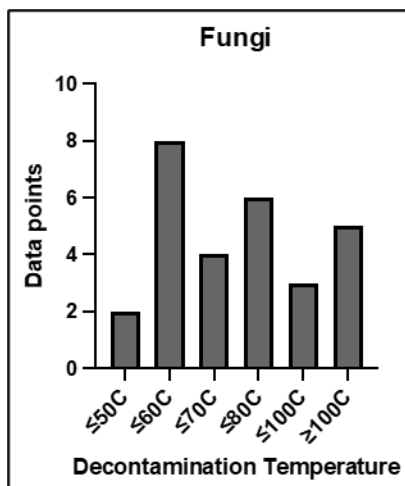


Figure 9 - Comparison of tested decontamination temperatures of fungi

3.3.6 Log Reduction

Regardless of decontamination parameters, log reduction information was captured in extraction, when data was present. In some instances, only presence or absence of subculture growth was recorded and did not include a numerical log reduction. Figure 10 shows overall log reduction data for hot air decontamination across all organism classes. Most articles were not successful in full decontamination, many only seeing a 0.5 log reduction in organism titer, however, a large number of articles did state ≥ 6 reduction or negative subculture, meaning no growth was observed following decontamination.

Log reduction was also plotted against decontamination temperature in order to see at what temperatures had the most success against all organism classes (Figure 11).

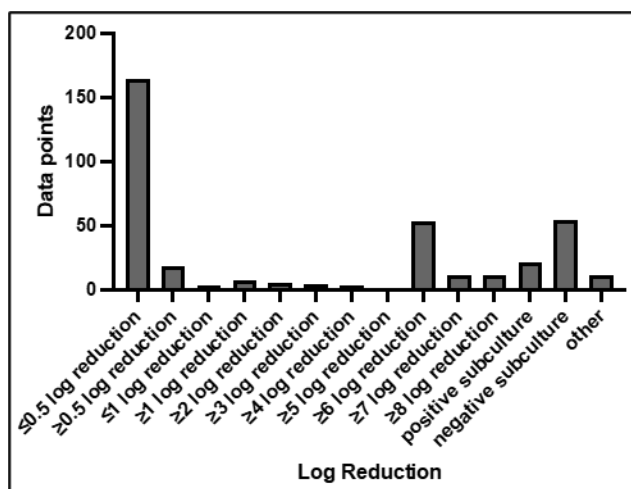


Figure 10 - Log reduction after dry heat decontamination across all organism classes

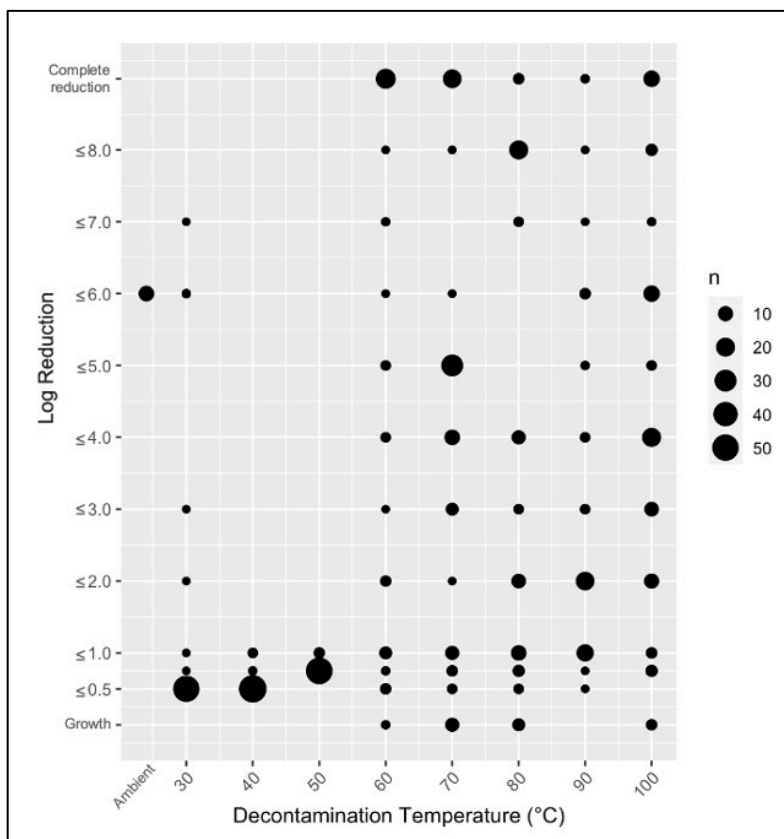


Figure 11 - Log reduction of pathogens (e.g., bacterial, viral, fungal) at various decontamination temperatures (°C); n = number of data points; complete reduction of a pathogen resulted in no growth at that temperature, whereas growth indicated failure of the temperature to inhibit growth

Figure 11 adds more context to the data displayed in Figure 10 and allows us to see that the majority of 0.5 log reductions occurred at low temperature range from 30-50°C and were derived from one particular publication yielding 144 data points. This publication investigated decontamination of avian influenza virus at various temperatures and RH, showing little log reduction at low temperatures (4). For the remaining data, once decontamination temperatures increased to above 60°C, a much wider range of log reduction is seen, a majority of articles report complete reduction of organism.

Outliers seen in the top left of the graph, high log reduction at low temperatures, are the result of a study of SARS-CoV-2 survivability on different materials. The virus was unable to survive on materials such as stainless steel, even at these moderate temperatures (5).

4. SUMMARY & NEXT STEPS

To capture data specific for hot air decontamination procedures effective against biological contaminants, the initial search discovered over 6000 articles of interest, and through review, a down select resulted in 110 articles for data extraction. The down selection criteria were implemented to ensure hot air decontamination was the focus and primary decontamination methodology. Studies were excluded if heating was conducted in liquid or autoclaved, as these methods incorporate steam or a moist environment which is out of scope for hot air decontamination. Other exclusion criteria included temperatures exceeding 121°C, organisms not of interest, or heating with something other than hot air. Excluded organisms (not of interest), were either classified as non-communicable or non-transmissible and are irrelevant to hot air decontamination on a plane, where the contaminant originates from patient transportation procedures.

The evaluation of data for hot air decontamination procedures toward biological organism of interest captured in this landscape survey are intended to help inform decontamination procedures effective in an airplane setting and will be compiled with data captured and consolidated in the Aircraft Decontamination Landscape Survey (AOS-23-0230). By gathering datapoints across multiple factors such as temperature, RH, time to decontamination, and the extent of decontamination, models can be built to predict the outcomes of these variables. While these models are undefined here, the data sets consolidated from this research provide the baseline decontamination needs for each organism or organism class. Additional information captured in the landscape survey will be included in further multivariate data analysis. Complete data analysis will be used toward informing predictive models used for protocol development of hot air decontamination. The robustness of the data will be determined by summarizing data gaps for categorical information used to inform a predictive model, and recommendations will be made regarding model validations either by in silico or wet lab testing.

5. RECOMMENDATIONS

1. Gregory Wickham, An investigation into the relative resistances of common bacterial pathogens to quaternary ammonium cation disinfectants, *Bioscience Horizons: The International Journal of Student Research*, Volume 10, 2017, hzx008, <https://doi.org/10.1093/biohorizons/hzx008>
2. Rabenau, H.F., Cinatl, J., Morgenstern, B. et al. Stability and inactivation of SARS coronavirus. *Med Microbiol Immunol* 194, 1–6 (2005). <https://doi.org/10.1007/s00430-004-0219-0>
3. van Netten, Chris et al. “Investigation and remediation of diesel converted trolley buses associated with extensive fungal growth and health complaints.” *American Industrial Hygiene Association journal* 58 10 (1997): 726-31
4. Guan, J., Chan, M. and VanderZaag, A. (2017), Inactivation of Avian Influenza Viruses on Porous and Non-porous Surfaces is Enhanced by Elevating Absolute Humidity. *Transbound Emerg Dis*, 64: 1254-1261. <https://doi.org/10.1111/tbed.12499>
5. Richter WR, Sunderman MM, Mera TO, O'Brien KA, Morgan K, Streams S. Evaluation of environmental conditions as a decontamination approach for SARS-CoV-2 when applied to common library, archive and museum-related materials. *J Appl Microbiol*. 2022 Apr;132(4):3405-3415. doi: 10.1111/jam.15468. Epub 2022 Feb 15. PMID: 35094472; PMCID: PMC9306959.

APPENDIX A. SYSTEMATIC LITERATURE REVIEW

A systematic literature review applies a rigorous process to identifying, screening, and reviewing scientific documents. These reviews present an unbiased assessment of the evidence by evaluating the strength of the evidence through a focused research question, evaluation of the quality of each study, and a quantitative pooled statistical analysis (known as a meta-analysis). A systematic literature review is different than a narrative review, in which authors typically describe a theory or opinion that is also supported by peer-reviewed literature but does not require a systematic collection and analysis of the science to provide inference about the value of the evidence.

Systematic reviews proceed through three phases: 1) literature identification and abstract screening, 2) full text review and quality assessment, and 3) synthesis of findings. While duplicate, independent review is the gold standard, reviews can use single, independent review for abstract screening and full text review to accommodate the project timeline. The process of the systematic literature review is outlined below.

A.1 Question of Interest

What decontamination methodologies are conducted for aircraft and aircraft relevant materials?

What are the associated organisms of interest (pathogens/simulants)?

- Landscape survey of current decon methods
- List of pathogens of interests along with surrogate models that could be used for validation
- Focus on ‘Hot Air’ and ‘Relative Humidity’

A.2 Abstract Review

a. DEFINE EACH TERM OF THE OUTCOME OF SYSTEMATIC REVIEW

- Decontamination-** Decontamination is a combination of processes that removes, destroys or neutralizes contaminants from a person or object to minimize the transfer of harmful materials, preventing or controlling infection or further contamination. Decontamination validation or verification is determined by a measured response of organism presence, growth or reduction in viability.
- Decontamination methods-** Processes used to create or promote sterilization or decontamination; Focus on “hot air” and “relative humidity”
- Organisms of interest-** Any organism with the potential of causing a negative pathology or pathogenesis (bacteria, virus, fungus); include relevant simulant list for these organisms of interest

b. DEFINE LIT DATABASES & SEARCH TERMS

- Database(s): Embase; DTIC; PMC (not in medline/ PubMed)
- Search Phrase(s):
TOPIC: see direct search files- Appendix B
AND TOPIC: see direct search files- Appendix B

- iii. Filter(s): English only, no abstract or review articles (will save for information gathering if relevant)
 - iv. Total N = ##### articles (add sections based on review process and total number of primary articles and for specific searches)
- c. IDENTIFY A REVIEW AND EXAMPLE PAPERS TO ORIENT EVERYONE**
Use these to orient everyone to what you're doing as well as do a quick practice of "I would include this one but not this other one". If disagreements, discuss why and make decisions about how to clarify instructions!
- d. DEFINE INCLUSION/EXCLUSION CRITERIA**
- a. **Inclusion** (use terms from subsection *A* above); Example: Articles that describe decontamination methodologies
 - b. **Exclusion**
 - i. Non-English language- Self explanatory
 - ii. Review/ OpEd- Abstract does not report data collected within the described study (i.e., primary data)
 - iii. No or Unclear methods- Poorly described methodologies (what is it?!); No process described
 - iv. Not applied with relevant pathogen- No organism mentioned or detailed
 - v. Other (***)please describe why in the Add a Note section at the bottom of the entry(***)- Doesn't quite fit but you're not sure of the correct box (please use sparingly)
- e. DEFINE QUALITY SCORING**
- i. How do you know an article is of high quality and one you will include?
 - 1. Useful for prioritizing data extraction in text reviews
 - ii. Some reviews don't do this but good to consider
- f. SET-UP COVIDENCE FOR ARTICLE REVIEW**
- i. Set-up account at Covidence.org using directions here:
<https://welch.jhmi.edu/databases?t=Covidence>
 - ii. To review abstracts:
 - 1. Click [**insert name of review**]
 - 2. Click on **Title and Abstract Screening** ribbon and click blue **Continue** button
 - 3. At the top of the page, click on **Show Criteria** to display Inclusion/Exclusion Criteria
 - 4. Read the abstract for each reference and determine if the article aligns with the underlined statement of the review's focus above
 - a. If abstract aligns well, select **Yes** to include this reference for full text review
 - b. If abstract meets any exclusion criterion in the table below, click on **Add a Note** below the abstract to list the criterion and select **No**
 - c. Don't use **Maybe**

5. Complete at least [insert min #] abstracts, more if you can!

g. CONDUCT SEARCH(ES) AND PULL ABSTRACTS INTO COVIDENCE

h. REVIEW ABSTRACTS

Split up identified abstracts among team

i. MEET TO REVIEW PROGRESS

Weekly meetings

CAPTURE DATA

- a. **DEFINE DATA FOR EXTRACTION-** What elements of information must be extracted from each article to answer the question of interest?
- b. **SET-UP DATABASE FOR EXTRACTION-** Covidence has this but Microsoft Excel can be used if EACH reviewer has their own spreadsheet. (will use excel)
- c. **EXTRACT DATA-**Do not mingle reviewers in data extraction, particularly if Excel

ANALYSIS

a. DETERMINE IF DESCRIPTIVE ANALYSIS OR META-ANALYSIS IS APPROPRIATE

Meta-analysis is only applicable to quantitative data.

Descriptive analysis is high level summaries and perhaps statistical summaries of quantitative info.

Outline and define 'Feasibility Metrics'

b. CONDUCT ANALYSIS

c. DERIVE INFERENCES

What are the high-level conclusions that you can make from this information?

What is the limitation of the information you received? What other info may exist that can supplement these data? What would a stakeholder who has done this for 25years say about this topic?

d. WRITE REPORT

APPENDIX B. EMBASE SEARCH TERMS AND COMBINATIONS

| No. | Query | Results | Date |
|-----|---|---------|----------|
| #18 | #16 NOT #17 | 7545 | 1-Jun-23 |
| #17 | #16 AND ('Editorial'/it OR 'Review'/it) | 580 | 1-Jun-23 |
| #16 | (#13 OR #14) AND [english]/lim AND [abstracts]/lim | 8125 | 1-Jun-23 |
| #15 | #13 OR #14 | 9082 | 1-Jun-23 |
| #14 | #3 AND #12 | 1693 | 1-Jun-23 |
| #13 | #6 AND #9 AND #12 | 7701 | 1-Jun-23 |
| #12 | #10 OR #11 | 3408053 | 1-Jun-23 |
| #11 | bacteri*:ab,ti OR fung*:ab,ti OR microb*:ab,ti OR spore*:ab,ti OR viral:ab,ti OR virus:ab,ti | 2965608 | 1-Jun-23 |
| #10 | 'fungus'/exp OR 'infectious agent'/de OR 'microorganism'/exp | 779353 | 1-Jun-23 |
| #9 | #7 OR #8 | 459866 | 1-Jun-23 |
| #8 | asepsis:ab,ti OR aseptic:ab,ti OR decontamina*:ab,ti OR clean*:ab,ti OR sanitiz*:ab,ti OR steriliz*:ab,ti OR disinfect*:ab,ti | 279269 | 1-Jun-23 |
| #7 | 'antiseptis'/exp OR 'decontamination'/exp OR 'disinfection'/exp OR 'heat sterilization'/exp OR 'instrument sterilization'/exp OR 'pressure sterilization'/exp OR 'communicable disease control'/exp | 231462 | 1-Jun-23 |
| #6 | #4 OR #5 | 875226 | 1-Jun-23 |
| #5 | fogging:ab,ti OR heat*:ab,ti OR 'hot air':ab,ti OR humid*:ab,ti OR moisture:ab,ti OR steam*:ab,ti OR thermal:ab,ti OR vapor*:ab,ti OR vapour*:ab,ti OR ((liquid NEAR/5 fog*):ab,ti) | 751092 | 1-Jun-23 |
| #4 | 'gas'/exp OR 'heat chamber'/exp OR 'heat'/exp OR 'high temperature'/exp OR 'humidity chamber'/exp OR 'humidity'/exp | 269653 | 1-Jun-23 |
| #3 | #1 OR #2 | 6377 | 1-Jun-23 |
| #2 | 'autoclave':ab,ti OR 'amsco 400':ab,ti OR 'amsco 600':ab,ti OR 'amsco c series':ab,ti OR 'amsco evolution':ab,ti OR 'gss p':ab,ti OR 'gss r':ab,ti OR 'steam sterilizer':ab,ti OR 'steam sterilizers':ab,ti | 2845 | 1-Jun-23 |
| #1 | 'autoclave'/de | 4968 | 1-Jun-23 |

LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMS

| | |
|------------------|--|
| AFRL | Air Force Research Laboratory |
| BSL | Biosafety Level |
| °C | Degrees Celsius |
| dsDNA | Double-stranded deoxyribonucleic acid |
| ssDNA | Single-stranded deoxyribonucleic acid |
| DTIC | Defense Technical Information Center |
| <i>E. coli</i> | <i>Escherichia coli</i> |
| Gram(-) | gram-negative |
| Gram(+) | gram-positive |
| JHU/APL | Johns Hopkins University Applied Physics Laboratory |
| PRISMA | Preferred Reporting Items for Systematic Reviews and Meta-Analyses |
| RH | Relative Humidity |
| dsRNA | Double-stranded ribonucleic acid |
| ssRNA | Single-stranded ribonucleic acid |
| ssRNA (-) | Negative (or Anti)-sense single-stranded ribonucleic acid |
| ssRNA (+) | Positive-sense single-stranded ribonucleic acid |
| <i>S. aureus</i> | <i>Staphylococcus aureus</i> |
| SARS-CoV-2 | severe acute respiratory syndrome coronavirus 2 |
| USAF | United States Air Force |