ENVIRONMENTAL IMPACTS OF ANIMAL EXPERIMENTATION

OPPORTUNITIES FOR CHANGE: THE NEW ST. PAUL'S HOSPITAL AND HEALTH CAMPUS

Progressive Non-Animal Research Society of British Columbia

About Progressive Non-Animal Research Society

The Progressive Non-Animal Research Society (PNARS) is a non-profit organization that brings the message of innovative, humane, biomedical breakthroughs to the health care professional/scientific community and supports emerging and established scientists in the fields of biomedical research, testing and training who use, or are interested in using, new approach methodologies (NAMs) – often referred to as non-animal methods.

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Executive Summary

Wastes and pollution generated from animal experimentation are recognized as a threat to environmental and human health. Millions of animal bodies are rendered as hazardous wastes requiring disposal, along with associated chemicals, drugs, bedding and laboratory consumables. Animal waste incinerators consume excessive amounts of fuel, release higher concentrations of air contaminants, and pollute the land and water, in turn jeopardizing human health. Diseases originating from animal laboratories represent substantial occupational and public health risks.

In the City of Vancouver, animal experimentation occurs at research facilities including the renowned St. Paul's Hospital, operated by Providence Health Care. The Progressive Non-Animal Research Society commissioned this report to assess environmental hazards associated with animal experimentation, entailing a review of the scientific literature, followed by discussion of potential wastes and pollution to be generated from biomedical research at the new St. Paul's Hospital & Health Campus.

We requested information from Providence Health Care and reviewed publicly available resources on environmental aspects of animal research at St. Paul's Hospital. Information was found to be non-existent in this regard, and despite high standards for sustainability, no references were made to the usage of animals in research, efforts to achieve the Three R principles nor efforts to mitigate related hazardous wastes and pollution. Understanding basic information on animal usage, disposal and wastes is foundational not only to public accountability, but to any meaningful evaluation of sustainability monitoring, mitigation and reduction of impacts to the environment and human health.

In Canada, innovative non-animal methods are advancing biomedical research, the Canadian Centre for Alternatives to Animal Methods, located at the University of Windsor in Ontario, being at the forefront. The development of the New St. Paul's Hospital and Health Campus offers a chance for the west coast of Canada to secure a place of leadership in sustainable non-animal medical research. We hope this assessment and recommendations provide value for stakeholders and impetus to further changing the way we conduct research at this new state-of-the-art facility as a model and standard for contemporary Canadian human-relevant science.

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Introduction

Opportunity for Change: St. Paul's Hospital

St. Paul's Hospital (SPH) is a renowned acute care, teaching and research hospital, and recognized as a global leader in health care. To integrate research, education and training, SPH has a partnership with the University of British Columbia (UBC) and other BC universities (City of Vancouver, 2017). In the City of Vancouver, animal experimentation occurs at SPH, UBC, Simon Fraser University, and other facilities (Kelly, 2019).

Providence Health Care (PHC) is a Vancouver-based not-for-profit society that owns and operates the SPH. In 2015, PHC and the provincial government announced that the current hospital located on Burrard Street would be relocated to a new state-of-the-art hospital on Station Street in the False Creek Flats. Currently, construction of the New St. Paul's Hospital and Health Campus (NSPH) is underway. The new hospital will be of great benefit to society, the City of Vancouver, British Columbia, and medical science.

In rezoning of the site for the NSPH, laboratory uses, including animal testing, are permitted under the City of Vancouver CD-1 By-law specific to the site (Kelly, 2019; City of Vancouver, 2022a). However, the transition to a state-of-the-art hospital and research facilities presents an ideal time and opportunity for PHC and SPH to take the initiative in shifting from animal experimentation toward sustainable modern methods. The timing is well suited given renewed commitments to environmental sustainability, feasibility of contemporary innovations and bolstered investment for the future of medical research. SPH has an unparalleled opportunity to position itself as a leader in human-relevant medical research and better contribute to meaningful scientific progress.

Purpose and Objectives

This report was commissioned by the Progressive Non-Animal Research Society to assess environmental hazards associated with animal experimentation. The report is intended to provide insights and recommendations for stakeholders involved, including the public, indigenous communities, non-governmental organizations, scholars and academic institutions, governments, politicians, scientific journals and funding agencies, the Canadian Council on

Animal Care, the City of Vancouver, the University of British Columbia, Vancouver Coastal Health and Providence Health Care.

The primary objectives of the Environmental Impacts of Animal Experimentation report are two-fold. The first objective is to summarize evidence of common environmental hazards and impacts produced by animal testing laboratory activities. Second, the environmental hazards of animal experimentation will be further discussed in the context of potential wastes and pollution generated from proposed biomedical research activities at the new St. Paul's Hospital & Health Campus located in Vancouver, British Columbia. The new St. Paul's Hospital & Health Campus is discussed to represent a Canadian opportunity for progress and leadership.

Scope of Work

The scope of work for the Environmental Impacts of Animal Experimentation report entails the following:

- Review of the scientific literature pertaining to environmental hazards associated with experimentation on animals, including resource consumption, wastes and pollution, public health implications, occupational health and zoonoses.
- Further review of any available documentation specific to Providence Health Care and St. Paul's Hospital related to the following:
    - commitments to environmental sustainability.
    - types of animal research, species used, and commercial services.
    - sewer discharge, specifically Hospital Pollution Prevention Bylaw.
    - biohazardous and biomedical waste and incineration (relevant BC Hazardous Waste Regulation, associated UBC guidance documents and manuals)
- Assessment of transparency and accountability of Providence Health Care research, specifically:
    - the inclusion, or any mention of, monitoring, assessment, and reduction of hazardous wastes and pollution from animal research practices.

- whether animal experimentation impacts and goals are incorporated within sustainability planning.
- whether reporting of animal numbers and usage are undertaken.
- acknowledgement or deliberation on alignment with the fundamental Three R Principles (replacement, reduction and refinement) of animal research.

- Preparation of a report outlining the above findings, in addition to discussion (e.g., metrics for progress, innovation and regulatory progress, and sustainable research in the context of human health), followed by final recommendations for stakeholders.

Background

The number of animals expended to experimentation worldwide is estimated at nearly 200 million animals every year. Evidence from the scientific literature suggests that the practice of animal research is a significant contributor to carbon emissions and environmental pollution (Cubitt & Sharp, 2011; Groff et al., 2014; Treherne, 2020; Treherne & Langley, 2021). Trends in the numbers of animals used are rising both globally and within Canada (Black et al., 2022; CCAC, 2023; CSHS, 2021; Ormandy et al., 2009; Taylor and Alvarez, 2008; Taylor and Alvarez, 2019); even despite increasing usage of more sustainable, animal-free alternatives (Groff et al., 2014; Meigs et al., 2018). Despite the current evidence and increasing trends in animal usage, environmental consequences have not yet been satisfactorily addressed (Groff et al., 2014).

Animal laboratories rely heavily on energy and resources, fossil fuels and incinerators. Pollution and wastes are generated throughout the lifecycle of animal research during husbandry, transport, care and feeding, experimentation, and final disposal. Disposal typically involves incineration of biomedical and hazardous wastes (i.e., animal carcases, excrement, bedding, and laboratory plastics and consumables) contaminated with toxins, chemicals, drugs, and pathogens. Evidence demonstrates exposure to gases associated with incineration contributes to health hazards including decreased life expectancy, reduced resistance to infections, hypertension, respiratory diseases such as asthma and bronchitis, cardiovascular diseases such as heart attack and stroke, cancer and mortality (Franchini, 2004; Groff et al., 2014).

Forces Accelerating a Paradigm Shift

Ethical considerations, enhanced scientific predictive methods, economic opportunity and environmental implications represent principal determinants of a global paradigm shift away from animal usage in research and toward scientifically defensible human-based approaches. The anti-vivisection movement has long been based upon ethical justifications (Meigs et al., 2018).

Scientific innovations are being stimulated by the urgent need to find effective solutions. Using animals in research has raised concerns of scientific merit, the plausibility of findings, reproducibility, and human relevance (Ellis et al., 2022; Groff et al., 2014; Meigs et al., 2018; Sun et al., 2022; Treherne & Langley, 2021; Wilkinson, 2019). Issues include low rates of blinded outcome assessment and randomization, low statistical power, high rate of statistically significant findings, publication bias and low publication rates (Ellis et al., 2022). The systems surrounding animal research play a role in fostering these problems. For example, academic incentives to engage in questionable research practices often lead to false positive findings in animal research (Ellis et al., 2022). Conversely, publication of valuable findings from non-animal studies are inhibited by peer-review journal associations due to 'animal-reliance bias' (Krebs et al., 2022). Animal-reliance bias occurs when journals request that animal data subsequently be provided to validate studies produced using nonanimal human-based approaches. This further acts as a barrier to scientific progress.

Economic drivers are being realized as opportunities for new business and markets, consumer acceptability, better and safer products, and more effective and rapid discovery (Meigs et al., 2018; Treherne & Langley, 2021). Economic consequences of incorrect results question maintaining outdated animal tests (Meigs et al., 2018; Wilkinson, 2019). In the development of drugs, the primary motivation to improve efficiency is the immense waste of resources, as over 90% of candidate drugs entering clinical trials fail to reach the market (Sun et al., 2022; Wilkinson, 2019).

In recent years, the environmental implications of animal research have been evaluated, demonstrating mounting support for a paradigm shift. Groff et al. (2014) provided an examination of the literature detailing findings of environmental impacts attributed to animal research and testing industries. Specifically, pollution to air, water, and soil, in addition to public

health concerns, and biodiversity losses. Evidence clearly suggests that "the environmental implications of animal testing must be acknowledged, reported, and taken into account as another factor in addition to ethical and scientific reasons weighing heavily in favor of moving away from allowing and requiring animal use in research and testing (Groff et al., 2014)."

Assessment of Environmental Hazards

Resource Consumption

Animal Usage

Global usage

Worldwide, a conservative annual estimate of the number of animals used for animal experimentation was 192.1 million in the year 2015 (Taylor and Alvarez, 2019). This estimate includes all mammals, birds, reptiles, amphibians, fish and cephalopods. Taylor and Alvarez (2019) reflect on their estimates of dogs (207,724) and monkeys (158,780) alone as "*both truly staggering, unsustainable figures that deserve urgent attention*." The total number of animals, as well as the estimated number of procedures carried out (80 million procedures), are both steadily increasing (Taylor and Alvarez, 2019).

Ellis and colleagues (2022) discuss the alarmingly low publication rate in animal research, meaning a large proportion of animals are used in studies which are never published. Further, publication bias, where decisions to publish are strongly dependent on whether a study found positive associations or not, is rampant (Ellis et al., 2022). Considering the 2015 worldwide estimate of 192.1 million animals, and referring to van der Naald's estimated percentage of the number of animals published as 26.3% (Ellis et al., 2022), this means 141.6 million animals (73.7%) in a single year were potentially used as part of unpublished studies. The annual number of laboratory animals used globally is conceivably higher today, as is the true number of animals never to be recorded in the published literature.

Canadian usage

The Canadian Council on Animal Care (CCAC) reports annually on the number of animals used in research and testing by *voluntarily* CCAC certified institutions in Canada. In 2021, there were 3,692,479 animals used by certified CCAC institutions (CCAC, 2022). The animals most used were mice (34.1%), fish (33.1%), and birds (12%). Studies *of a fundamental nature in science relating to essential structures or functions* used the largest proportion of animals (33.9% representing 1,251,563 animals). Studies for *medical purposes, including veterinary medicine, that relate to human or animal diseases or disorders* represented 17%

(656,739 animals), while studies for the *development of products or appliances for human or veterinary medicine* represented 19% (722,931 animals) (CCAC, 2022).

The CCAC Animal Data Reports do not show animal use trends over the years, questioning supposed commitments and transparency in achieving the Three Rs principles (*replacement, reduction and refinement*) (Black et al., 2022). It is important to look at annual trends to gain a better understanding of whether animal use is generally increasing or decreasing over time. Fortunately, academic scholars and non-profit originations have evaluated the numbers to give an overall picture of the trends and where Canada sits regarding the Three Rs.

Although a large decrease occurred from 2020 to 2021 (due to the pandemic and a large chicken-related study in 2020), the overall trend in the total number of animals used in Canada is increasing (Black et al., 2022; CCAC, 2023; CSHS, 2021; Taylor and Alvarez, 2019). In a global context, from 2005 to 2015, Canada moved from sixth to the fourth largest animal user, after China, Japan and the US; with a notable increase in animal use (Taylor and Alvarez, 2019). Furthermore, Canada was identified as a top user of dogs (3rd) and monkeys (5th) (Taylor and Alvarez, 2019). According to the CCAC Animal Data Report for 2021, 10,055 dogs and 6,818 nonhuman primates were used in research in Canada, both increased from 2020.

Several scholars point to the fact that the statistics on the number of animals used in research in Canada are incomplete since they are based on voluntary surveys from only CCAC-accredited institutions (Black et al., 2022; Stewart, 2021; Taylor and Alvarez, 2019). This means animal use numbers from private companies are not tabulated and are unknowable. Therefore, the number of animals used for research in Canada is higher than the figures outlined above, making any meaningful evaluation of trends and performance of the Three Rs problematic.

Consistent animal usage despite increased usage of alternative approaches

Despite widespread implementation of validated alternative approaches (e.g., *in vitro and in silico* technologies) and establishment as a modern industry, gross animal use has not changed as an outcome (Meigs et al., 2018). Meigs et al. (2018) outline several reasons for this including additional regulatory testing demands and an overall increase in research. For example, focusing on the sector of basic biological research and biomedical research, the numbers of animals per publication continued to decrease in the last 10-20 years due to use of human stem cells or in vitro and in silico approaches. However, in this case, the total numbers of animals are stable

since the number of researchers in this space are increasing. Previously, Ormandy et al. (2009) attributed the increasing global trend in the use of animals is research to the rise in usage of genetically-modified animals. Meigs et al., (2018) noted that reductions in animal use may be overcompensated by the numbers of animal used in basic research, particularly genetically modified mice. Although alternative approaches have not changed gross animal use, regular usage of animal-free methods surpasses public perception, and performance is often so high that traditional methods have been rendered obsolete (Meigs et al., 2018).

Gap in resource usage compared to advanced methods

Animal tests are often too costly, take too long, and give misleading results (Meigs et al. 2018; Treherne & Langley, 2021). Using toxicity tests as an example, Groff et al. (2014) provide two examples demonstrating the wide gap in resource use when comparing traditional animal methods to modern methodologies having better or similar predictability. Standard toxicity tests may use 6,000 to 12,000 animals and take years to complete. For screening of 300 chemicals, animal toxicity tests required 30 years and consumed $2 billion, while the Environmental Protection Agency's ToxCast program completed the same in only 5 years using 600 rapid, automated in vitro tests of equal or greater predictive value (Groff et al., 2014).

Similarly, carcinogenetic testing using the *in vivo* (animal) method lasts at least 24 months (rats) and 18 months (mice), consuming a minimum of 400 animals. Due to low predictability of the animal methods, the U.S. National Cancer Institute (NCI) drug discovery and development arm developed non-animal methods for carcinogenicity as well as anti-HIV drug efficacy and cell toxicity tests (e.g., 60 human tumor cell line to screen compounds for anti-tumor effects).

Energy

The energy requirements of research animal facilities are up to ten times that of offices per square meter (Cubitt & Sharp, 2011; Groff et al., 2014). Increased energy demands are primarily attributed to the need for total fresh air exchanges for ventilation. The rate of exchange of large volumes of air is significantly greater than for a standard laboratory (Groff et al., 2014; Treherne & Langley, 2021). Additional sources of energy consumption include environmental and space needs of the animals, barrier protection from outside pathogens, indoor air quality,

lighting, and power-intensive equipment (Treherne & Langley, 2021). Collectively, this amounts to elevated energy consumption and increased carbon emissions.

Chemicals and Drugs

A wide array of chemicals is used throughout animal research for sanitation, disinfection, sterilization, animal care and research procedures. Toxic substances include irritants, corrosive substances, asphyxiants, neurotoxins, reproductive and developmental toxins and carcinogens. Compared to animal-free methods, these chemicals are likely used more frequently, for longer durations, or in larger quantities (Groff et al., 2014).

Drugs are also tested and consumed in large quantities in animal research. Emerging technologies such as integrated microfluidic synthesis and screening for drug discovery have potential to reduce adverse environmental impact from synthetic chemistry by requiring minimal compound (Treherne & Langley, 2021).

Plastics and Consumables

Animal research laboratories require an extensive assortment of plastic and consumable products[1]. In addition to lab furnishings and large equipment, lab animal products include the following:

- Personal protective equipment (e.g., gloves, masks, disposable garments, hoods, eye protection, and booties).
- Animal care equipment and supplies (cages, animal hydration systems and hosing, feed, bedding).
- Enrichment supplies (e.g., chewing devices, refuge canopy, toys, nesting sheets).
- Identification supplies (e.g., ear tags and tattoo kits).
- Handling equipment (e.g., animal restraints, jackets and harnesses; Elizabethan, cervical and pillow collars; animal guide catch poles/hooks).

[1] Two examples of lab animal product retailers: https://perotech.com/lab-animal-products/ and https://www.sai-infusion.com/

- Surgical equipment and supplies (e.g., surgical platforms; anesthesia systems, breathers, filters, inhalation chambers; infusion pumps; needles and syringes; tubing; catheters; gavages and feeding needles; blood collection tubes and vials).
- Euthanasia systems and supplies (e.g., gas chambers, regulators, flow meters and CO_2 cylinders).

Wastes and Pollution

Non-Hazardous and Hazardous Wastes

Chemical and biological wastes and pollution generated by animal research facilities are extensive, the most prominent being the millions of animal bodies. In addition to animal carcasses, wastes include animal excrement, bedding, excess feed, caging, needles, syringes, and gavages (Groff et al., 2014).

Hazardous wastes are routinely generated and disposed from animal research. Predominantly, animal carcasses that are contaminated with toxic, radioactive or hazardous chemicals, viruses, or infectious diseases are deemed chemically and/or biologically hazardous. Hazardous chemical wastes may include disposal of mercury, methane, and cyanide, as well as known or possible carcinogens including benzene, arsenic, formaldehyde, lead, DDT, and chloroform (Groff et al., 2014).

Incineration and Environmental Pollution

Incineration is the preferred disposal method for hazardous wastes, resulting in air emissions such as particulate matter, nitrogen dioxide, sulfur dioxide, and carbon monoxide (Groff *et al.*, 2014). Wastes that are both chemically and biologically hazardous are difficult to dispose and facilities able to accept them are limited (Groff et al., 2014).

Particulate matter and gasses produced from the incineration of animal carcases containing experimental chemicals, drugs and toxins mixed with laboratory supplies and animal bedding contribute to air pollution. Incineration has been deemed an environmental concern as the process requires high fuel consumption to maintain temperatures, disposal of remaining ash to landfills, and significant contributions to air pollution (Groff et al., 2014). Global warming pollutants generated from incinerators contribute to smog, acid rain and ozone formation (Groff

et al., 2014; Lam et al., 2010). Incineration releases particle pollution, toxic ashes, and toxic wastes to the air including dioxin, mercury, and lead. Additionally, it is known to contaminate local soil, vegetation and groundwater.

Animal waste incinerators particularly have been shown to release higher concentrations of toxic contaminants in air. For example, studies demonstrated stack gases having greater concentrations of heavy metals as well as polycyclic aromatic hydrocarbons (PAHs), when compared to standard medical waste incinerators (Groff et al., 2014). PAHs are persistent in the environment and deemed as carcinogenic substances to humans. Humans are predominantly exposed to PAHs by breathing in contaminated air (Groff et al., 2014).

In 2010 Metro Vancouver proposed a 500,000-tonne-per-year waste-to-energy (WTE) facility, in addition to the already existing WTE facility in Burnaby[2], as part of a solid-waste management plan. Researchers from the University of British Columbia made the case that the addition would sharply increase emissions of mercury, lead, cadmium, and dioxins from solid waste disposal in Metro Vancouver (Lam et al., 2010). The researchers concluded that waste reduction and diversion is the most ideal solution for Metro Vancouver through diverse programs and incentives, in order to have the least impacts to the environment and human health.

Animal testing also contaminates waterways and public drinking supplies as water treatment facilities can't filter out all drugs, hormones and chemicals (Groff et al., 2014). The presence of antibiotics, endocrine disruptors, cytotoxic cancer drugs and other drugs are problematic for aquatic animals and may contribute to human health effects (Groff et al., 2014).

Human Health Implications

Human exposure to contaminants generated from the incineration of hazardous wastes produces adverse health effects (Franchini, M, 2004). People are exposed to contaminants released from incinerators via inhalation, contact with soil or water, or ingestion of food and water (Figure 1) (Groff et al., 2014; Valberg et al., 1996).

[2] In 2016, concerns were raised of health risks to local communities from the Burnaby incinerator.

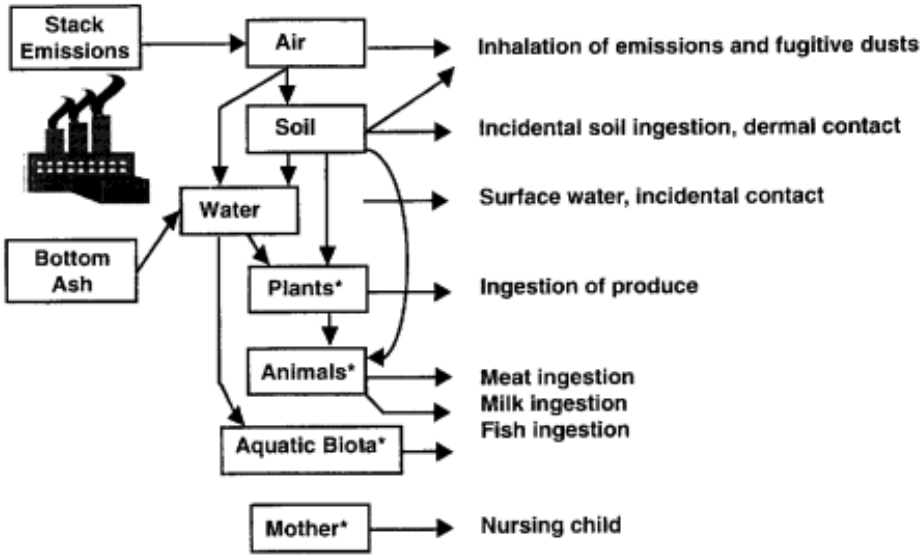

Figure 1 - Conceptual model of exposure pathways between municipal solid waste incinerators and potential human receptors. Adopted from Valberg et al. (1996).

Evidence demonstrates exposure to gases associated with incineration contribute to health hazards including decreased life expectancy, reduced resistance to infections, hypertension, respiratory diseases such as asthma and bronchitis, cardiovascular diseases such as heart attack and stroke, cancer and mortality (Franchini, 2004; Groff et al., 2014). Local communities near incineration facilities are impacted. Additionally, distant communities can be affected since some pollutants (e.g., dioxins, furans, and mercury) can persist for long periods of time and can be carried long distances in the environment (Groff et al., 2014; Thornton et al., 1996). The National Research Council (NRC) Committee on Health Effects of Waste Incineration has identified particulate matter, lead, mercury, and dioxins and furans as the incinerator pollutants with potential to cause the largest health effects and number of deaths (Groff et al., 2014).

Occupational Health and Zoonoses

Workplace exposure to pathogens from laboratory animals, such as those used for biomedical research, is well documented as an occupational health risk with the potential of becoming a serious public or global health threats (Hankenson et al., 2003; Louz, 2005; Weigler, 2005; Pham-Thanh, 2022; Jiang et al., 2023). In 2007, Cheng *at al.* warned of "the possibility

of the re-emergence of SARS and other novel viruses from animals or laboratories and therefore the need for preparedness should not be ignored (Cheng at al., 2007*).*"

Post pandemic research after the emergence of COVID-19 demonstrates the plausibility of the laboratory origin hypothesis (Sirotkin and Sirotkin, 2020; Deigin and Segreto, 2021; Segreto and Deigin, 2021; Segreto et al., 2021; Hassan ; Ruiz-Medina et al., 2022). Distinctive molecular clues from SARS-CoV-2 point to a common research procedure, known as viral serial passage, which uses a live animal host. This practice manipulates viral genomes to force a jump between species in a laboratory, much faster than the same molecular processes can occur in nature (Sirotkin and Sirotkin, 2020). Evidence deliberated by Segreto et al. (2021) suggested COVID-19 potentially emerged from "the use of humanized mice for the development of SARS-CoV-2 in a laboratory environment." Humanized mouse strains, or genetically engineered mice, utilized for SARS-CoV-related research is well documented (Segreto et al., 2021).

The Center for Arms Control and Non-Proliferation calculated the odds that any given potential pandemic pathogen might leak from a lab to be one in four (Klotz and Sylvester, 2014; Sirotkin and Sirotkin, 2020). As with the increased research into coronaviruses amplifying the odds of escape, the 1977 HqN1 Swine Flu, widely cited as originating from a laboratory leak, was attributed to increased research interests into influenza vaccines (Sirotkin and Sirotkin, 2020). It is clear the risk of outbreaks from experiments using laboratory animals to study viruses such as these far outweigh any benefit, as pandemic consequences are catastrophic.

Providence Health Care and St. Paul's Hospital

The research enterprise of PHC is known as PHC Research Institute (PHCRI), which is affiliated with the University of British Columbia and Simon Fraser University. Internationally recognized research areas of expertise and programs include HIV/AIDS, heart and lung diseases, kidney disease, gastro-intestinal diseases, psychiatry, geriatrics, long covid and more (Providence Research, 2022).

The City of Vancouver was contacted on February 18, 2022, in a freedom of information request for definitive information on future development plans and laboratory usage pertaining to

chemicals and wastes produced, managed, transported, disposed, or emitted to the environment. The City of Vancouver transferred the request to Providence Health Care.

Specific questions were:

- *Please provide procedural or best practice documents related to laboratory practices, chemicals used, biohazards and disposal.*
- *What types of experiments will be conducted at the facility?*
- *What animals will be used?*
- *What chemicals are used?*
- *Where will disposal occur and what are the waste procedures.*

The following response was provided by PHC, in a letter dated September 20, 2022: *"PHC has completed a search for records. However, as the future development of our new site is still several years away and the uses of the new facility have not yet been finalized, we do not have any documents that would respond to your request."* Public facing information and resources on current practices or future plans in terms of environmental aspects are limited to non-existent, and no reference is made to the usage of animals in research. Our information query underscores issues with transparency and does not satisfy any understanding of efforts to achieve the Three R principles or any efforts to mitigate related hazardous wastes and pollution. As such, any information in the following sections was derived from sources where available.

PHC Commitments to Environmental Sustainability

PHC is committed to environmental sustainability which is demonstrated in current operations and future planning of the new facility. However, the unsustainable practice of animal experimentation takes place within research laboratories at the existing SPH and the site of the new facility has been zoned such that animal experimentation can continue. The new state-of-the-art facility represents an ideal opportunity for change.

From an environmental perspective, transitioning away from animal use in research would help PHC reduce resource consumption, biohazardous wastes, and emissions including offsite incineration, thereby strengthening alignment with sustainability commitments. Specifically, the following municipal and internal policy and planning documents outline guiding principles and specific commitments pertaining to environmental sustainability:

St. Paul's Hospital and Health Campus Policy Statement

Rezoning Policy for Sustainable Large Developments

Mission: Forward – Providence Health Care Strategic Plan

(see also: Providence Research Strategic Plan)

PHC Energy & Environmental Sustainability

Environmental Sustainability Policy (POLICY #BCD-12-11-40000)

2021 Climate Change Accountability Report Providence Health Care

PHC GreenCare 2020 Environmental Performance Accountability Report (EPAR).

The strategic plan developed by PHC to guide the next seven years outlines five foundational principles, one being *sustainability*: protective financial and environmental stewardship. The principle states "…reducing our environmental footprint to achieve — and hopefully exceed — national benchmarks for sustainability, green initiatives, and minimal impact." Furthermore, one goal of the sustainability principle is to achieve the goals laid out in the Provincial Clean BC Plan. Reduction of harmful wastes and pollution by transitioning away from outdated animal experimentation is necessary to satisfy PHCs foundational principle of *sustainability*. This can be achieved by adopting best available technology and practices, while concurrently leading the pathway to transforming medical research for the benefit and protection of people and animals.

Types of Research and Animals Used

Innovation and leadership are embedded in research, and it should be first highlighted that there are examples of PHC researchers working to advance cutting edge animal-free technologies such as organs-on-chips. Collaborative research is leveraging lung-on-a-chip technology to mimic human lungs, which is being developed (Mitacs, 2022a,b) and applied (Mitacs, 2022c). The drive for this innovation is denoted as a pressing need for the discovery of therapeutics to treat chronic obstructive pulmonary disease (COPD), which has been hindered by outdated and costly animal models (Mitacs, 2022a,b,c).

Notwithstanding the celebrated progression of human-relevant innovation, other research conducted at or affiliated with PHCRI still employs animal models. Moreover, the Heart and Lung Institute at SPH has dedicated animal testing services available for contract, such as pre-clinical studies [3]. This includes pre-clinical models involving rodents and rabbits [4]. In 2020, pre-clinical animal experiments were conducted for amyotrophic lateral sclerosis (ALS) disease, Marfan's syndrome, muscular dystrophy, cardiovascular disease, chronic obstructive pulmonary disease, and emphysema (HLI, 2021).

PHC does not release animal use numbers, something UBC has been doing since 2010 (UBC, 2022). UBC undertakes responsible transparency by providing information on the total number, species groups, degree of invasiveness and purpose of use of animals involved in research. UBC also releases its comprehensive assessment report by the Canadian Council for Animal Care. PHC and SPH, despite close affiliation with UBC, does not undertake the same commitment to transparency, therefore making it difficult to understand animal usage. Review of the literature provides insight into some species used for PHC affiliated research, including **rodents** (Chamberlain et al., 2009; Donen et al., 2022; Hirota, 2013; Hiebert et al., 2013; Mitacs, 2022d; Shen et al., 2017; Shen et al., 2018; Tsutsui et al., 2021; White et al., 2019; Xue et al., 2022), **sheep** (Baylis et al., 2017; Dong et al., 2022), **pigs** (Kim at al., 2020; Mitacs, 2022d; see also HLI, 2021), and **dogs** (White et al., 2020). Generally, animal types may be comparable to those used at UBC [5], given close affiliation and exchange of researchers, but quantitative information is unknown.

At the very least, it is critical to acknowledge and account for resource consumption, wastes and emissions associated with animal experimentation within the applicable environmental sustainability documentation and reporting. Reporting animal use numbers, at a minimum, would benefit the transparency and accountability of PHC research. Advancement of the widely recognized Three Rs (*replacement, reduction* and *refinement*) is likely not effective without monitoring and data for assessment of progress. Communication in terms of

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[3] Services available for contract at SPH Heart and Lung Institute: https://www.hli.ubc.ca/our-services/

[4] Pre-clinical models on rodents and rabbits: https://www.hli.ubc.ca/our-services/pre-clinical-models/

[5] Animal types used at UBC: https://animalresearch.ubc.ca/about-ubc-animal-research/numbers-animals

environmental sustainability is the first step to understanding and reducing environmental impacts.

Sewer Discharge

In 2018, the Hospital Pollution Prevention Bylaw was introduced by the Greater Vancouver Sewerage and Drainage District. In accordance with the bylaw, hospitals located in Metro Vancouver (within the Greater Vancouver Sewerage and Drainage District) are required to develop and submit a pollution prevention plan every five years (first reports were due January 31, 2021), along with yearly progress reports detailing actions taken to implement the pollution plan. The bylaw applies to PHCs institutions including SPH.

The intent of the bylaw and pollution plans is to enable hospitals to assess their operations and eliminate or reduce pollutions at the source. The bylaw indicates that hospitals produce waste that, when discharged or discarded into sewers or drains, may impact sewers, sewage facilities, human health and the environment, and therefore it is desirable to regulate the discharge of wastes from hospitals. Core requirements to be addressed within the plan include biomedical waste, unused drugs, formaldehyde, and silver-rich solutions.

Details of the bylaw can be found here: Bylaw to Regulate the Discharge of Waste from Hospitals (Bylaw No. 319)

Biohazardous and Biomedical Waste and Incineration

Hazardous waste is regulated in British Columbia by the BC Hazardous Waste Regulation. UBC identifies waste streams commonly produced from biological research including microbiological waste, biomedical waste, sharps, toxins, pathological waste, non-indigenous waste, non-human primate waste, pharmaceutical waste, and controlled substances (UBC, 2020a). Waste is packaged and tagged appropriately depending on the stream for collection and transport to an offsite facility.

UBC specifies a procedure for Animal Carcasses Disposal defining proper disposal for uncontaminated or contaminated animal carcasses (UBC, 2020b). Animal waste is a form of biomedical waste, defined in the BC Hazardous Waste Regulation, 2009. Similarly, animal bedding is considered biomedical waste under the regulation. Disposal of biomedical waste at

regular landfills or waste-to-energy incineration facilities is prohibited by Metro Vancouver and under the BC Hazardous Waste Regulation.

Animal carcasses and associated hazardous wastes generated by SPH are likely transported by a contracted commercial disposal company to a licenced biomedical waste incineration facility. Information is not available to elucidate where animal research carcasses and associated wastes generated by SPH are transported for incineration, whether it is local or outside of British Columbia. However, the biosafety manual of affiliated UBC provides insight as it also refers to off-campus generators such as research centers and hospital sites. Pathological waste is transported by the company, Forever in Peace, to Mission, BC for incineration. Biomedical waste is shipped by the disposal company, Stericycle, for incineration in Alberta (UBC, 2020a). Stericycle is a medical waste management company operating globally, with social responsibility commitments to protection of human health and the environment. A report published by Health Care Without Harm assessed whether Stericycle historically lived up to its mission. One of the recommendations of the environmental and health assessment report was to phase out the use of incineration and adopt available cleaner and safer waste disposal technologies (HCWH, 2002).

Discussion

Implications for Environmental and Human Health

Through all phases associated with animal research (i.e., animal rearing, experimentation and disposal), resources are consumed, and wastes and pollution are generated (Figure 2). Elevated energy consumption results in increased carbon emissions. Transportation fuel is used for moving animals and equipment from breeding facilities, between various laboratories and research facilities, and finally for disposal. Incineration of hazardous wastes consumes high amounts of fuel and pollutes the air, land and water, in turn jeopardizing human health.

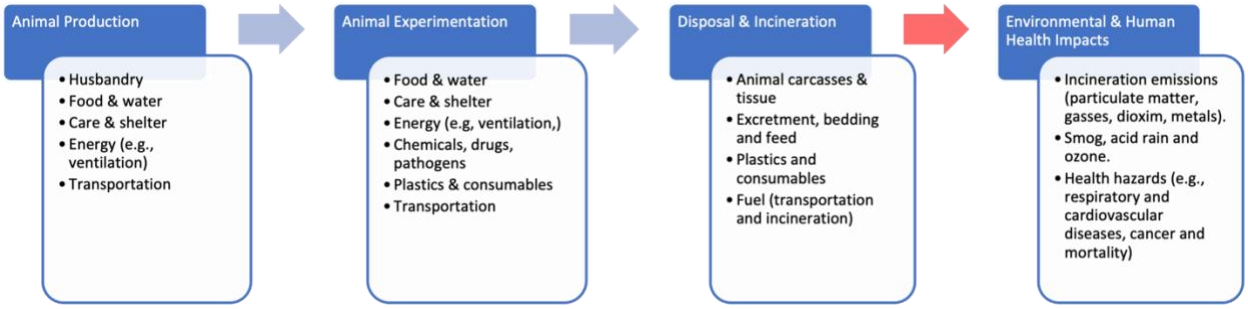

Figure 2 – Resources consumed, wastes and pollution generated and costs to environmental and human health attributed to the animal research lifecycle.

Metrics for Progress

In Canada and abroad, the Three Rs (*replacement, reduction and refinement*) are widely recognized as a foundation for programs and legislation. In order to evaluate the progress of these principles, quantitative metrics are necessary. Taylor et al. (2008) wrote "*Relatively few countries collate and publish animal use statistics, yet this is a first and essential step toward public accountability and an informed debate, as well as being important for effective policy-making and regulation*". This holds true for the purposes of understanding environmental impact. In order to adequately delineate the carbon footprint of an animal research centre or sector, it is essential to record and understand basic information on animal usage, disposal and wastes. Knowing this basic data is foundational to assessment and characterization of carbon emissions and pollution and subsequent programs and policy formation aiming to monitor, mitigate or reduce impacts to the environment and human health.

PHC and SPH have high standards for sustainability. Yet in review of all public facing information and resources, no reference is made to the usage of animals in research. Specifically, no information is made available on the scientific or ethical standards of animal subjects, on animal usage numbers, nor efforts to achieve the Three R principles or any efforts to mitigate related hazardous wastes and pollution. In order to have a complete representation of wastes and impacts, the contribution from animal research needs to be considered and made transparent for any meaningful evaluation of sustainability monitoring and progress.

Innovation as a Driver of Sustainability

Technical advances in human-relevant testing and research have successfully demonstrated increased efficiency, reliability, welfare, cost-effectiveness and environmental sustainability. Therefore, testing and research is already a promising sector of opportunity to contribute to environmental sustainability and to reduced greenhouse gas emissions and climate impacts. Additional support through regulation and funding is needed to further innovation.

Innovation is driving change, which is further necessitated by converging global crises. For example, Treherne & Langley (2021) contend that the Covid-19 pandemic and climate disruption together have disrupted drug discovery by forcing emerging technologies, and that this could ultimately reduce the carbon footprint of discovering drugs. Novel more predictive solutions like organoids grown in vitro replace the use of animals and are therefore reducing the carbon footprint of cancer drug discovery (Treherne, 2020).

The Canadian Centre for Alternatives to Animal Methods (CCAAM) at the University of Windsor is an example of academic excellence and broader progress in medical research. Moving forward, governments, academic institutions and organizations can shift away from reliance on outdated animal testing and fully harness the potential of human-relevant science. Canada, British Columbia, PHC and similar new entities such as the UBC Biomedical Engineering facility have this opportunity, positioning as leaders in innovative medical and scientific research.

Regulation as a Driver of Sustainability

There is no regulation of animal experimentation oversight in Canada. At the fundamental level, oversight regulation is urgently needed. In addition, regulation to phase out animal experimentation, is imperative to further encourage innovation and change. Concrete action plans specifying proactive targets are an essential impetus to phasing out animal experiments and stimulating animal-free methods. Regulation for adequate oversight of animal experimentation in Canada as well as regulation for phasing out the use of animals both play a role in beneficially contributing to sustainability goals.

The Government of Canada is beginning to phase out the use of animals in some categories with two major achievements in the spring of 2023: cosmetic testing was officially

banned and further steps were taken to phase out toxicity testing. First, amendments made to the *Canadian Environmental Protection Act 1999 (CEPA)* became law on June 13th, 2023, including provisions around toxicity testing. The CEPA amendments specify goals to eradicating animal toxicity testing in Canada and establishes firm requirements and timelines in transitioning to use of alternative methods. This supports the Liberal governments commitment to phase out toxicity testing on animals by 2035. Second, amendments to the Food and Drug Act became law on June 22, 2023, prohibiting testing of cosmetic on animals and sale of cosmetic products tested on animals.

Toxicity testing is also being phased out elsewhere. The US EPA has similarly committed to phase out all toxicity testing on animals by 2035, backed by legislation amendments to the *Toxic Substances Control Act.* In California, a law was passed in 2022 banning toxicological testing of harmful chemicals on dogs and cats. With the European Union at the forefront of eliminating cosmetics testing, in total 41 countries have similar bans or restrictions.

Beyond toxicity testing, other countries are making major strides to replace animal experimentation with modern methods. Subsequent to the 2010 EU Directive to phase out all animal experiments, the European Parliament recently adopted a resolution in 2021 "on plans and actions to accelerate the transition to innovation without the use of animals in research, regulatory testing and education."

In the United States, new regulatory changes are expected to expedite drug discovery and make life-saving medications more affordable. Recently congress passed the FDA Modernization Act, adding a section 'Animal Testing Alternatives' which amends FDA regulatory requirements of animal testing for drugs. The Federal Food, Drug, and Cosmetics Act redefines 'nonclinical tests' to include human-relevant testing methods such as cell-based assays, microphysiological systems (such as Organ-Chips), or bioprinted or computer models. This is a significant achievement in protecting the health of Americans. Health Canada needs to similarly take action in updating regulatory processes for contemporary drug discovery.

For Canada, while headway is being made in the cosmetic and toxicity testing industries, further regulation, government support and investment are needed in order to achieve broader protections and progress encompassing other categories of research. Experts from the University

of Dalhousie and the Canadian Society for Humane Science argue that the current non-legislated oversight system for animal research, administered by the Canadian Council on Animal Care, needs major reform (Black et al., 2022). They highlight that this system fails not only to incentivize replacement of animals, but also fails adequate protection for those bred, harmed and killed (Black et al., 2022). The researchers conclude that national legislation is needed in Canada, as it is an important step to significant change in animal protection and the development and implementation of non-animal methods (Black et al., 2022).

Sustainable Research Safeguards Human Health

Human illnesses are increasingly being directly connected to climate change. A new report in the medical journal, The Lancet, calls climate change the greatest global threat to human health, highlighting that it is much more than just an environmental issue (Romanello et al., 2022). Recently, Canadian health care is mobilizing action on climate change. Canada's chief public health officer, Dr. Theresa Tam, stated:

> *"calling really for a shift in our collective mindset, to think about climate change not just as an environmental issue, but one of the most important public health threats that we're facing."*

The climate crisis is a human health emergency. This begs the question, in a quest to protect human health through testing and research, why are nearly 200 million animals being expended through inefficient, resource intensive experiments and subsequent incineration and pollution of our air, land and water? Especially considering most animal studies are not published and superior options are available and achievable. Ironically, medical research centres are utilizing a tool that contributes to the very health challenges we seek to address.

PHC and the NSPH are at the forefront of care and innovation, dedicated to enhancing the health and wellbeing of British Columbians. Therefore, PHC operations have an even greater role and responsibility in taking action to prevent and reduce human illnesses. This includes reducing environmental impacts from animal research wastes and pollution. We ask PHC to lead the way on the path that is moving forward and which is being altogether endorsed by the public, science, policy, economics, and the health of ecosystems, animals and humanity. Protecting the environment is a priority for protecting human health.

Recommendations

Recommendations for PHC and SPH

Become a leader in human-relevant medical research

- Take advantage of the opportunity to shift away from animal experimentation, positioning as a leader in sustainable modern human-relevant medical research. Renewed commitments to environmental sustainability, successful technologies and the increased funding accompanying the transition to the new state-of-the-art hospital and research facilities together present ideal conditions to move away from unsustainable research practices.

Identify experts to champion an alternative methods centre at the New SPH

- Identify a professional academic expert or team in human-relevant methods to champion a center for human-centrical innovation at the NSPH. This may be akin to The Canadian Centre for Alternatives to Animal Methods (CCAAM) at the University of Windsor.

Assess environmental impacts of animal research at PHC

- Engage the Energy and Environmental Sustainability team (EES) of PHC to consider, monitor and address the environmental impacts of animal research undertaken at PHC facilities. Further deliberate benefits of animal-free research as a sustainable solution.

Address questionable research practices in animal research

- Address the problem of academic incentives leading to questionable research practices in animal research. Ellis et al. (2022) recommends the adoption of registered reports, in the same manner as clinical trials, and comprehensive reporting guidelines as two essential strategies to align scientific incentives with rigorous methodology.

Incentivize animal free research

- Implement programs, provide support, funding and research grants in order to promote projects which are carried out using non-animal methods by PHC researchers. This will facilitate sustainable research and the path forward to better science while protecting the planet and humans.

Maintain records and transparency on environmental aspects of animal research

- Ensure sufficient record keeping and deliver transparency in terms of environmental aspects associated with animal research (i.e., procedures, hazards, resource consumption, wastes, pollution, emissions, and at minimum: animal numbers, biomass and disposal information). Further, transparency is necessary for efforts to achieve the Three R principles, in addition to assessment and reduction of hazardous wastes and pollution from animal research practices.

Account for animal experimentation in environmental sustainability commitments

- Incorporate resource consumption, wastes and emissions due to animal experimentation into environmental sustainability planning and policy. Accounting for environmental aspects of animal experimentation will strengthen alignment with both the Three R principles and PHCs sustainability commitments.

Report on progress toward the Three R principles

- Advise upon how PHC is working toward achieving the Three R principles. PHC would benefit by making this information publicly available.

Recommendations for the City of Vancouver

Consider the environmental impacts of animal experimentation

- The City of Vancouver must consider the environmental and human health impacts of animal experimentation. Record keeping of all environmental aspects of animal research, particularly animal numbers, biomass and disposal information, is essential.

Implement mandatory record keeping and transparency on environmental aspects of animal research

- Maintaining records and transparency in terms of environmental aspects associated with animal research is important to protecting our air, land and water and the people of Vancouver. Records may include procedures, hazards, resource consumption, wastes, pollution, emissions, and at minimum: animal numbers, biomass and disposal information. As a city, this information is necessary for tracking our progress toward the Three R principles. Furthermore, it allows the opportunity to identify, mitigate and reduce hazardous wastes and pollution from animal research practices.

Incentivize animal free research in Vancouver

- Promote the usage of animal free methods at research facilities during development and sustainability planning. Sustainability planning must consider animal experimentation.

Provide SPH's Pollution Prevention Plan and progress reports

- Please accept this information request to Metro Vancouver for SPH's Pollution Prevention Plan and progress reports, to date, submitted in accordance with the Hospital Pollution Prevention Bylaw. Also requested is any other information related to animal numbers and environmental aspects of animal research.

Establish needs for further study regarding animal testing policy in Vancouver

- Establish the needs and requirements of further study for policy regarding animal testing in Vancouver. The end of the memorandum *Response to animal testing correspondence received in relation to the New St. Paul's Hospital rezoning application* states: "If Council determines the need to create policy regarding animal testing in Vancouver, then it is recommended that the issue be further studied and brought forward comprehensively to apply equally to all sites within the city (Kelly, 2019)."

Recommendations for Scientific Journals

Require registered reports and reporting guidelines in animal research

- Address the problem of academic incentives leading to questionable research practices in animal research. Ellis et al. (2022) recommends the adoption of registered reports, in the same manner as clinical trials, and comprehensive reporting guidelines as two essential strategies to align scientific incentives with rigorous methodology.

Address 'animal-reliance bias' in peer review

- Address 'animal-reliance bias' where journals reviewers request that animal data are provided to validate findings from human based studies (Krebs et al., 2022). Strategies to combat this bias may include peer review training and accreditation, two-stage review and open peer review (Krebs et al., 2022).

Align peer review with achieving the Three R principles in research

- Implement framework to align the peer review process with the Three R principles.

Recommendations for the Government of British Columbia and Government of Canada

Require assessment of progress toward the Three R principles

- Amend the Agreement on the Administration of Agency Grants and Awards by Research Institutions, Section 4.4: Research Involving Animals, such that facilities are required to track and evaluate progress toward achieving the Three R principles.

Allocate funding for innovation centres and associated research

- Funding for innovation is necessary to stimulate a transition and gain economic, scientific, and environmental benefits. British Columbia and Canada must direct funding toward animal-free research as well as to establishing new dedicated research centres.

Reform non-legislated oversight system through appropriate regulation of animal experimentation in Canada

- Currently, there is no regulation for any oversight of animal experimentation in Canada. Experts from the University of Dalhousie and the Canadian Society for Humane Science argue that the current non-legislated oversight system for animal research, administered by the Canadian Council on Animal Care needs major reform (Black et al., 2022).

Implement legislation phasing out animal experimentation in Canada

- Regulation is essential to phasing out all categories of animal experimentation in Canada. For example, in order to protect the health of Canadians, Health Canada must take action in updating the regulatory process for contemporary drug discovery, similarly to the FDA Modernization Act in the United States. More broadly, akin to the goals of the 2010 EU Directive, Canadian policy must move toward ending the use of animals in research, regulatory testing and education.

“Climate action is public health action. Let’s boldly act together and act now.”

Dr. Theresa Tam,

Chief Public Health Officer of Canada

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