

Advisory Report for the Health Sciences Association of British Columbia and the National Union of Public and General Employees on Respiratory Protection During Care of Influenza Patients

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About the Author

This report was prepared by a team of consultants at Resource Environmental Associates Limited (REA). REA is a professional firm of 30 personnel established in 1991 that specialises in occupational and environmental health and safety, and has significant experience in environmental / non-pharmaceutical infection control.

The principal author of this paper is John H. Murphy, President, Resource Environmental Associates. Mr. Murphy holds Bachelor of Science, Master of Health Science (Occupational Hygiene), and Master of Business Administration degrees from the University of Toronto. He is a Certified Industrial Hygienist, Registered Occupational Hygienist, and Graduate Member of the United Kingdom Institute for Occupational Safety and Health. He has been a full-time practising occupational hygienist since 1985, during which time he has also published and presented on a variety of technical and public policy subjects in occupational health and safety, and served as a member on various professional and governmental advisory bodies, including the Ontario Workplace Safety and Insurance Board's Occupational Disease Panel, and the Ontario Minister of Labour's Joint Steering Committee on Hazardous Substances in the Workplace. He is currently a member of the advisory council for the Centre for Research Expertise for the Prevention of Musculo-Skeletal Disorders based at the University of Waterloo.

Mr. Murphy's personal experience in the subject matter of this paper is summarized below :

- Qualified by the Ontario Labour Relations Board as an expert witness on respiratory protection.
- Respiratory protection program consultant, and project manager in charge of respiratory fit testing clinics for several SARS Alliance hospitals in the Greater Toronto Area, during the 2003 SARS outbreak.
- Consulting team project lead for investigation and remediation of the only two health care sector Legionnaire's disease outbreaks in Canada over the past two decades (Grand River Hospital, 2002, and Seven Oaks Home for the Aged, 2005).
- Project consultant on numerous environmental infection risk assessment and control assignments undertaken for several hospitals and homes for the aged in southern Ontario.
- Project lead for a workplace influenza transmission risk assessment undertaken under contract to the Ontario Ministry of Government Services (2008), and principal author for the project report entitled *Protecting Personnel from Pandemic Influenza* (REA Project 13188, August 2008).
- Advisor to school boards, municipalities and private sector corporations on environmental control measures for reducing risks of influenza transmission.
- Thought-leader advisor to a major multinational manufacturer of health care supplies.
- Various speaking engagements and presentations on environmental infection control topics (including pandemic influenza, Legionnaire's disease, aspergillosis), to professional audiences at conferences and seminars organized by the American Industrial Hygiene Association and the Occupational Hygiene Association of Ontario.

Executive Summary

In August 2009, the Health Sciences Association of British Columbia (“HSABC”) and the National Union of Public and General Employees (“NUPGE”) retained Resource Environmental Associates Limited (“REA”) to provide commentary and advice with respect to scientific positions, statements and recommendations made in the following documents with respect to usage of N95 respirators versus procedure / surgical masks for protection of health care workers providing care to influenza patients:

- (a) “Prevention and Control of Influenza during a Pandemic for all Healthcare Organizations”, prepared by the Public Health Agency of Canada (“PHAC”), draft in-progress version dated July 16, 2009, and
- (b) “SHEA Position Statement: Interim Guidance on Infection Control Precautions for Novel Swine-Origin Influenza H1N1 in Healthcare Facilities”, released by the Society for Healthcare Epidemiology in America, dated June 10, 2009, and

In these documents, both PHAC and SHEA take the position that N95 usage is warranted only when performing procedures that generate substantial quantities of respiratory aerosols, and that N95 respirators are unnecessary for routine patient care.

In this paper we describe and cite the relevant science with respect to influenza transmission by respiratory aerosols, and the effectiveness of various types of respiratory protection equipment. This information is the basis for our critique of the PHAC and SHEA positions, as well as the basis for our recommendations with respect to appropriate respiratory protection for personnel providing care to influenza patients.

While not proven conclusively, there is now a considerable body of evidence, from various lines of viral disease aerosol transmission and survival research, animal experiments, and case reports, to suggest that inhalation of non-visible aerosols containing influenza virus (i.e. *exposure*) can cause disease transmission. Diligent use of well-fitting NIOSH-approved high efficiency particulate aerosol filtering respirators (e.g. N95) when providing care within a 2 meter zone of an influenza patient will result in significantly reduced *exposures* to respiratory aerosols, in comparison with using no respiratory protection at all, or using only surgical or procedure masks. Reducing inhalation exposure to respiratory aerosols should in turn reduce incremental risks of contracting influenza in providing patient care in the proximal atmosphere.

Our conclusion is that PHAC and SHEA are incorrect in asserting that N95 respirator use is warranted only for procedures generating high concentrations of respiratory aerosols. We are also of the opinion that there are factual errors, misstatements and unsubstantiated assertions in both the PHAC and SHEA documents.

We recommend the use of N95 respirators by health care workers to the extent practicable whenever those workers are within a 2 meter zone of an influenza patient.

1.0 Introduction

1.1 Background

In August 2009, the Health Sciences Association of British Columbia (“HSABC”) and the National Union of Public and General Employees (“NUPGE”) retained Resource Environmental Associates Limited (“REA”) to provide commentary and advice with respect to information contained in documents issued by two organizations regarding utilization of personal protective practices and equipment by health care workers (“HCWs”) when providing care to patients with suspect or confirmed influenza-like illness (“ILI”) during an influenza pandemic.

Specifically, HSABC and NUPGE sought our opinion with respect to scientific positions, statements and recommendations made in the following documents with respect to usage of N95 respirators versus procedure / surgical masks:

- (c) “Prevention and Control of Influenza during a Pandemic for all Healthcare Organizations”, prepared by the Public Health Agency of Canada, draft in-progress version dated July 16, 2009, and
- (d) “SHEA Position Statement: Interim Guidance on Infection Control Precautions for Novel Swine-Origin Influenza H1N1 in Healthcare Facilities”, released by the Society for Healthcare Epidemiology in America, dated June 10, 2009, and

1.2 Objectives of this Paper

The objectives of this paper are as follows:

1. To present a synopsis of the scientific information relevant to understanding the current debate on the relative significance of visible and non-visible respiratory aerosols in the transmission of influenza.
2. To comment on the type of respiratory protection equipment that is appropriate for minimizing inhalation HCW exposure to respiratory aerosols.
3. To identify in documents (a) and (b) referenced above any statements that we deem to be factual errors, or mischaracterizations of information contained in sources referenced by the document.

4. To provide our opinion with respect to the circumstances where N95 respirators should be used and worn by HCWs when providing patient care to persons with influenza-like illness.

1.3 Organization of this Paper

This paper begins in Section 2.0 by briefly describing factors that we believe influence professional and public policy recommendations for utilization of non-pharmaceutical personal protective measures and equipment in relation to influenza.

The paper then turns in Section 3.0 to a discussion of what is known (and not known) with respect to potential modes of transmission for seasonal influenza. This is important because advice on protective measures reflects beliefs concerning the strength of evidence for different modes of transmission, and the relative importance of each mode. Our characterization of the case “for” and “against” each mode of transmission is summarized in Section 4.0.

Section 5.0 presents what we consider to be the implications of the above for respiratory protection device recommendations for HCWs when providing care to influenza patients.

Sections 6.0 and 7.0 provide our commentary on the positions stated in the PHAC and SHEA documents, respectively, and identify specific instances of apparent factual discrepancies and inaccurate characterization of the contents of publications cited therein.

2.0 Considerations in Evaluating Recommendations for Utilization of Non-Pharmaceutical Personal Protective Measures and Equipment

The acts of formulating and evaluating recommendations for utilization of personal protective measures and equipment involve consideration of a range of factors, such as:

- regulatory requirements
- scientific and technical information
- marketplace availability
- economic utility

The process of formulating and evaluating recommendations involves weighing, judging, and assigning different levels of importance to many different pieces of information

within each category, as well as deciding how to weigh each category against the other in final decision-making.

2.1 Statutory and Regulatory Requirements

In an occupational health context as well as an infection control context, statutory and regulatory instruments often prescribe protective measures. However, at present in Canada there are no explicit regulatory requirements concerning the use of personal protective measures and equipment for reducing risk of influenza transmission in an occupational or healthcare setting. There are, however, clear statutory duties placed upon employers in all Canadian jurisdictions to take all reasonable precautions for the protection of workers, as well as sufficient occupational health and safety case law to judge what is and is not “duly diligent” in this context. The duty to take “reasonable precautions” exists whenever there is a reasonable contemplation that harm may occur, regardless of the frequency (or rate) with which harm might occur, the potential severity of harm, and whether or not the risk is inherent in the work.

2.2 The Role of Scientific and Technical Information

To evaluate the adequacy of recommendations with respect to occupational non-pharmaceutical protective measures against influenza, we believe it is important that there be an accurate understanding of:

- potential modes of transmission for influenza
- the case “for” and “against” the significance of each mode of transmission in relation to common health care delivery activities and settings
- evidence relating to the theoretical effectiveness of the control measures, assuming proper utilization, and assuming imperfect utilization
- the quantity and quality of empirical evidence as to the efficacy of control measures for the envisioned applications
- the practicality of control measure implementation

2.3 Marketplace Supply

Constraints on the ability to adequately source or deploy desired equipment and supplies can limit the implementation of recommendations. However, it is our belief that the most appropriate way of dealing with supply or logistical constraints is to formulate a multi-tier strategy for use of personal protective measures and equipment that starts with the best feasible option, and then proceeds to the “next best” option, and so on. This is essentially the “hierarchy of controls” principle applied specifically within the personal protective category of the hierarchy.

2.4 Economic Utility

In the discipline of economics, “economic utility” is the concept of creating the greatest good or greatest value for the greatest number of persons using a given level of resources. This concept is sometimes an explicit, but more often an implicit influence on occupational health and safety policy making and resource allocation.

It is our opinion that non-articulated economic utility assumptions are strongly influencing the current scientific and public health dialogue on the significance of aerosol transmission for influenza, and the need to implement measures for respiratory protection. However, consideration of economic utility issues in relation to this issue is beyond the scope of this paper.

2.5 Decision-Making in the Context of Imperfect Information

There are several ways in which persons and organizations make decisions in the context of imperfect information in relation to risk.

One approach is to adopt precautions despite uncertainty as to existence and the magnitude of the risk. In recent years, this has been called the “precautionary principle”, but more colloquially has been referred to for decades as “better safe than sorry”.

Another approach is to elect *not* to take action until the existence and magnitude of the risk is well understood and characterized. In some cases this approach may be influenced by the need to discern the appropriate risk management actions, ensure their effectiveness, and avoid inefficient deployment of resources. In other cases, risk management actions and their effectiveness are understood or predictable with varying degrees of certainty, and there can be a variety of reasons for preferring inaction.

A treatment of these different approaches to occupational health and safety policy decision-making is beyond the scope of this paper, but in light of the subject matter we believe it is important to be mindful of the fact that over the past century in North America there have been several instances where, before taking action to control a hazard, public health authorities, governments and employers have demanded the accumulation of substantial proof of harm, in the form of illness or death, before taking action to reduce risk of harm. The final report of the Campbell Commission criticized governments and health care institutions for adopting this type of decision-making standard for protection of HCWs from SARS.

It is also important to bear in mind that protective standards are often set without reference to any articulated level of risk, or consensus on what constitutes acceptable risk.

Arguably, when faced with uncertainty, there should be an onus on public health authorities, governments and employers to provide convincing “proof of protection” that their precautionary measures are effective and sufficient, as opposed to an expectation that there be “proof of harm” before mandating precautionary measures.

3.0 Discussion of Postulated Modes of Transmission for Influenza

Much has been written and published on the postulated modes of transmission for influenza. The modes of transmission are commonly referred to as “droplet transmission”, “contact transmission” (direct and indirect), and “airborne transmission” or “aerosol transmission”. While these descriptors are commonly used, there are no generally accepted or standard definitions for these concepts, and a review of their usage in the scientific literature and by public health authorities, as well as our own experience, suggests that different users conceptualize the modes of transmission in different ways.

For this reason, and the fact that assumptions regarding mode of transmission influence decisions relating to protective measures, we consider it important to begin this paper by presenting a diagrammatic model (Appendix) that illustrates our understanding of the postulated modes of person-to-person transmission of influenza. Rather than using conventional terminology, our model portrays transmission utilizing the physical forms of respiratory liquids or solids in which the viruses are initially contained, and the paths these materials follow between the host and the target.

3.1 Forms of Respiratory Discharges

The model identifies two physical forms of respiratory liquids or solids germane to controlling person-to-person transmission of influenza.

The first form of release is discharge as a respiratory tract aerosol [A1], from the nose (during a sneeze, simply exhaling or as a result of an aerosol generating medical procedure [“AGMP”]) or mouth (during coughing, talking, breathing as a result of an AGMP), or both. We use the word “aerosol” to mean all liquid or solid particles of all

sizes expelled from the nose or the mouth by sneezing, coughing, talking, exhaling or AGMPs. As such, it includes all different size ranges of particles¹.

The second form of virus release is discharge or removal from the mouth or nose [N1] in a form that is not an aerosol – namely contained in bulk liquid mucous or saliva, or dry material (e.g. nasal crusts). “Discharge” refers to all forms of release except “removal”, the latter referring to actions such as nose picking, sticking a finger into the mouth, or clinical procedures such as nose swabbing.

Our model generically identifies factors that affect the quantity of virus discharged by a person as aerosol [F1], and discharged or removed as non-aerosol [N1]. These include patient-specific factors, medical care practices, and the presence of source control measures. Specific examples of these are described in Table 1 (Line 1708) of PHAC Annex F, July 17 09 Draft, under the heading “Higher Transmission Risk” factors for the category relating to the “Infectious Agent / Infected Source”.

Our model also postulates that “Total virus discharge is positively correlated to the number of dischargers (i.e. infected persons), and their respective quantities and frequencies of discharge” [T1]. Assuming uniformity in application of control measures, an individual HCW’s potential total exposure would be expected to be positively correlated to the “total discharge” of virus in aerosol and non-aerosol forms, the HCWs proximity to the sources of discharge, and the total amount of time the HCW spends being exposed.

3.2 Forms, Characteristics and Behaviour of Respiratory Aerosols

Discharged respiratory aerosols consist of a mixture of visible particles [A2] and non-visible particles [A3] of various sizes (e.g. which is typically the case when generated by a sneeze), or simply non-visible particles (e.g. which is often the case for coughs, talking and exhalation).

Different types of respiratory discharges generate different quantities and size distributions of liquid particles.

3.2.1 Sneeze Aerosols

¹ Our use of “aerosol” includes the particulates referred to in the PHAC document as “droplets”, “airborne particles”, “droplet nuclei”, or “aerosol particles”.

A sneeze is estimated to generate up to 40,000 aerosol particles. Measurements have found that between 20% and 60% of the initially generated particles are larger than 100 microns, and on this basis it has been estimated that particles having an initial size larger than 100 microns should typically constitute between 95% and 99% of the liquid discharged by a sneeze².

Researchers have measured influenza virus in sneeze aerosol discharge³. It is likely that there is significant variability in concentrations from sneeze-to-sneeze, person-to-person, and as a function of the severity and phase of illness (e.g. higher concentrations during times of higher virus shedding).

If the concentration of virus in the sneeze droplets is uniform, then the concentration of virus in the population of droplets comprising the sneeze discharge would logically also be uniform (i.e. the number of virions per microlitre of fluid), and if that were the case, then between 20% and 60% of the virus would be contained in droplets larger than 100 microns. The presumption that this is true leads to the conclusion that most of the "virus dose" associated with a sneeze is contained in the droplets larger than 100 microns, and that very little of the "virus dose" is contained in droplets smaller than 100 microns. This idea appears to have influenced thinking on the relative levels of virus dosage (and risk of contracting illness) received as a result of exposure to large aerosol droplets versus non-visible aerosols, and hence the relative significance of "droplet transmission" versus "aerosol transmission".

However, in fact it is not known whether the concentration of virus is uniform across the population of droplets discharged by a sneeze. The total population of droplets discharged by a sneeze are comprised of a combination of liquids originating from different locations along the respiratory tract⁴ (e.g. sinuses, trachea, bronchioles), which may have different concentrations of viruses. Also, the formation of droplets of different sizes relates to the aerodynamic features of different parts of the airway. Consequently, it is possible that there are lower concentrations of influenza virus in larger droplets generated from fluids at locations expected to have lower mucosal virus concentrations (e.g. sinuses, mouth), while higher virus concentrations may be typical of smaller droplets generated from fluids at locations where mucosal virus concentrations are expected to be higher in an infected person (e.g. the bronchioles). This hypothesis has not been subjected to any research evaluation that we are aware of, but it is not an implausible hypothesis given the aerodynamic features of the airway and what is known

² Cole et al (1998), Dugid (1946).

³ Mubareka et al (2009)

⁴ Morawksa et al (2009)

about the relative susceptibility of different respiratory tract epithelial tissues to infection by different types of viruses.

When considering the potential difference in virus concentration associated with exposure to large droplets versus non-visible aerosols, it is also important to understand that at typical room temperatures and relative humidities, virtually the entire population of particles larger than 50 microns (i.e. visible droplets) will be converted by evaporation within seconds of discharge to particles smaller than 5 microns. In other words, within a few seconds of a sneeze, virtually all of the viruses present will be in the form of non-visible aerosol particles. Consequently, for a sneeze, the proportion of expelled virus in droplets larger than 100 microns is unlikely to be as important to the prediction of HCW "virus exposure" resulting from a patient's sneeze as the mass distribution in the initial population of droplets would suggest.

3.2.2 Cough Aerosols

A cough is estimated to generate between approximately 900 and 2100 particles. Measurements have found that there is significant variation in "cough to cough" size distribution, with anywhere from as little as 1% to as many as 99.9% of the initially generated particles being larger than 8 microns.⁵ The droplet concentrations of coughs are significant lower than the droplet concentrations of sneezes.⁶ As with sneeze aerosols, it is likely that there is significant variability in concentrations from cough-to-cough, person-to-person, and as a function of the severity and phase of illness.

The particle size / mass distribution / virus distribution / evaporation issues discussed above for sneeze aerosols are also applicable to cough aerosols, but to a lesser degree because coughs discharge a much smaller fraction of large particles than do sneezes.

3.2.3 Aerosols Released When Talking

Talking has been measured to generate between approximately 100 and 7000 particles⁷. The ambient droplet concentrations associated with talking on the order of 10 to 1000 times lower than the concentrations associated with coughs.⁸

⁵ Chao et al (2009), Weber et al (2008), Brankston et al (2007).

⁶ Chao et al (2009)

⁷ Chao et al (2009). In relation to this measurement, "talking" is defined as "counting from 1 to 100, loudly and slowly, ten times, with a pause after each number."

⁸ Chao et al (2009)

The particle size / mass distribution / virus distribution / evaporation issues associated with aerosols generated by coughing apply equally to aerosols generated by talking because the size ranges and skews of their particle size distributions are similar.

3.2.4 Aerosols Released by Exhalation

Ordinary exhalation also generates respiratory aerosols, most of which are under 5 microns, with a larger fraction smaller than 1 micron⁹.

3.3 The Fate of Visible Respiratory Aerosol Particles

Visible respiratory aerosol particles suffer one of four fates: (1) they evaporate and convert into droplet nuclei; (2) they impact upon persons or surfaces in their direct flight path, or fail to do so; (3) they stop in mid-air before hitting any target and fallout; or (4) they are inhaled by persons nearby. Each process is described below.

3.3.1 Evaporation

Under typical indoor relative humidity and temperature conditions, liquid particles expelled from the respiratory track begin to evaporate from the instant they are created.¹⁰ Some authors have suggested that these particles could increase in size following discharge, but most droplets discharged from the respiratory tract do not increase in size under typical indoor relative humidity and temperature conditions¹¹. An increase in size requires either (i) net condensation of ambient air moisture onto the droplet (which will not happen at relatively humidity levels less than 100%), or (ii) collisions between droplets that cause them to merge together and form a larger droplet (which may happen to some degree).

Evaporation rapidly reduces the aerodynamic diameter of visible respiratory particles. If the particle's aerodynamic diameter is reduced to about 50 microns, it is no longer visible to the unaided eye, and therefore no longer a "visible particle".

The reduction in diameter caused by evaporation is accompanied by a simultaneous reduction in the mass of the particle, which in turn continuously alters the ballistic behaviour of the particle (causing continuous reduction in velocity), and also its terminal settling velocity (causing the settling velocity to become progressively slower, which in

⁹ Chao et al (2009), Morawska et al (2009)

¹⁰ Weber et al (2008), Beggs (2003), Chao (2009)

¹¹ Beggs (2003), Weber et al (2008)

turn further reduces the fraction of particles that are still liquid droplets when they fall onto a surface).¹²

3.3.2 Impact

In the micron size range, particle impact on targets in the direct flight path is governed by the particle's ballistic behaviour, much in the same way as common everyday objects like baseballs. "Ballistic behaviour" simply means movement of the particle through the air toward a target (a person or otherwise), propelled by the kinetic energy imparted upon discharge. Ballistic behaviour occurs primarily in a zone up to approximately 60 cm from the point of large particle discharge¹³. This travel distance limit is imposed by the fluid resistance of the air, which slows and eventually stops particles.

The ballistic behaviour of visible respiratory aerosols is relevant to the postulated infection mechanism whereby expelled airborne respiratory droplets make ballistic impact upon the conjunctival membranes, and translocate to target tissues via the lacrimal duct and sinuses (what is often called "droplet transmission"). ***Specifically, the fluid resistance of air in combination with the aerodynamic diameter of particles places a limit upon the range of distances at which "droplet transmission" and inhalation of visible particles can occur – specifically, not beyond 60 cm from the point of emission.***

Once a ballistic particle stops in air, its subsequent movement is determined by the combined effect of ambient air currents and the force of gravity.

3.3.3 Fallout by Gravity

In conditions of complete or virtually still air (which includes the absence of convective air currents, and hence is rarely the case in healthcare settings), a micron-sized particle falls under the influence of gravity at a speed determined primarily by the fluid resistance of the air, and the particle's aerodynamic diameter and density¹⁴.

The typical upper limit size for a droplet generated by sneeze is on the order of 200 microns, but particles with a maximum size of approximately 100 microns are more prevalent¹⁵. The terminal settling velocity for a 100 micron droplet (assuming unchanging aerodynamic diameter) is approximately 0.3 meters per second in typical

¹² Beggs (2003)

¹³ Weber (2008)

¹⁴ Stokes Law.

¹⁵ Beggs (2003), Duguid (1946).

indoor temperature and relative humidity conditions. Therefore, a constant 100 micron droplet would take 5 seconds to fall to the floor from a starting height in air of 1.5 meters.

However, a 100 micron droplet comprised solely of water evaporates in approximately 1.3 seconds at 50% relative humidity and 22 degrees C¹⁶. Therefore, a 100 micron droplet would not be expected to fallout to the floor, but instead would evaporate to form a droplet nucleus (i.e. a "dry"¹⁷ particle with a diameter under 5 microns, comprised of virions, desiccated biomolecules, and cellular fragments). Particles below 5 microns effectively never "fallout" under the influence of gravity because the fluid resistance of air that they encounter combined with air currents overcomes the downward force of gravity¹⁸, and as a result these very small particles remain suspended until removed from the airstream by other mechanisms (such as filtration or static attraction to surfaces).

3.3.4 Inhalation

For a visible respiratory particle to be inhaled, another person needs to be in close proximity to the source of discharge (under 60 cm), for the reasons explained in Section 3.3.3 above, and the particle needs to be no larger than about 70 to 100 microns¹⁹. Particles larger than 70 to 100 microns are not readily inhaled because the force of air inspiration into the mouth or nose is generally not strong enough to entrain such "large" particles. The majority of inhaled particles in the size range of 10 to 100 microns are deposited in (i.e. captured by) the sinuses and trachea, with the smaller end of the distribution trapped predominantly in the trachea²⁰.

The location of deposition in the respiratory tract is relevant to the presumed potential for inhalation exposure to cause infection, because influenza viruses are known to infect some types of respiratory epithelial cells and not others. It is known that for influenza A virus to infect a cell, that cell must have a sialic acid-based biomolecule on the cell membrane that functions as a specific receptor size for the surface protein(s) of the virus²¹. If the cells of the tissues that comprise the "landing site" for the virus-laden droplet lack the virus-specific receptor, the virus cannot infect those cells²². Therefore, if

¹⁶ Beggs (2003)

¹⁷ Technically the particle would not be completely "dry" since the presence of humidity in the air would result in the retention of some moisture within the particle, but the particle would not longer be what is ordinarily thought of as a "liquid".

¹⁸ Tellier (2006). This can also be demonstrated by calculating the terminal settling velocity.

¹⁹ Weber (2008)

²⁰ Lippman (1990)

²¹ Weber (2008)

²² Van Ryan et al (2007)

the sinuses and trachea have few or no specific receptors for a particular type and strain of influenza virus, those tissues would not become infected, despite the deposition onto the tissues of virus-laden droplets.

It is known that the common types and strains of seasonal influenza principally infect the epithelial cells of the bronchioles and trachea, and can also infect the alveoli²³. The severity of disablement and risk of death from influenza is related to the extent and severity of infection of the trachea, bronchioles and particularly the alveoli. Seasonal influenza can also reportedly infect the sinuses and larynx, but infection of these tissues does not cause disablement or death.

Since visible respiratory droplets continuously evaporate from the instant they are generated (see Section 3.3.3 above), the small fraction of inhaled droplets larger than 50 microns that might be inhaled will continue to evaporate and reduce in aerodynamic diameter as they proceed through the airway of the person who has inhaled the droplets. Reduction in aerodynamic diameter during passage through the airway would be expected to result in a higher fraction of such particles depositing at further distances down the respiratory tract than would be expected on the basis of the initial aerodynamic diameter.

3.4 Fate of Non-Visible Respiratory Aerosol Particles

Particles having an aerodynamic diameter under 50 microns are generally not visible to the unaided eye. Inhaled particles beneath this diameter are deposited at different locations along the respiratory tract, as a function of particle diameter. Particles that are not inhaled by persons in the vicinity of the emitter are progressively dispersed throughout the air volume. These mechanisms are described below.

3.4.1 Deposition in the Respiratory Tract

Inhaled particles in the range of 10 to 100 microns are deposited mainly in the sinuses and throat. This is referred to as the "nasopharyngeal" size range. Inhaled particles in the range of 3 to 10 microns are deposited mainly in the trachea and bronchioles. Inhaled particles under 3 microns are deposited mainly in the alveoli, and a fraction may also be expelled again without being deposited.

²³ Tellier (2006), Van Ryan et al (2007)

A visible droplet that starts out at 50 microns loses virtually all of its water content within 0.3 seconds of discharge. Those of 10 microns evaporate in under 0.02 seconds²⁴. The resultant droplet nuclei are all below the nasopharyngeal size range. Consequently, non-visible respiratory aerosol particles that are inhaled deposit in the trachea, bronchioles and alveoli. This relationship between particle size and deposition locus along the airway is relevant to the disease transmission mechanism, since these non-visible particles are of a size that results in delivery directly to the epithelial tissues of the trachea and bronchioles, which are known to be susceptible to influenza infection²⁵.

3.4.2 Dispersal

In any given situation, only a small fraction of the total population of non-visible aerosol particles expelled by a person will be inhaled by other persons. In the "proximal atmosphere" (which for our model we define as a three dimensional zone within 2 meters of the emitter), this is a consequence of the geometry of aerosol discharge. Respiratory aerosols are dispersed in three dimensions, rendering only a small fraction of the particles available for inhalation in the breathing zone of persons nearby. In the "distal atmosphere" (which for our model we define as anywhere beyond the "proximal atmosphere"), only an exceedingly small fraction of the original population of particles would theoretically be available for inhalation, and only if (i) atmospheric translocation was possible (via ventilation systems or passive air currents), and (ii) sufficient time elapsed for translocation to occur by mixing and air movement.²⁶

3.5 Relationship Between Proximity to Source and Virus Exposure

We are not aware of any research that has attempted to systematically quantify changes in airborne virus concentration at different distances from the point of respiratory discharge. This would be of interest however, because (a) the relationship between distance from the point of aerosol discharge and the instantaneous ambient airborne concentration of viruses caused by the discharge may not be the general curvilinear decline that might be predicted, and (b) better understanding the relationship may help to better refine controls. Two possible concentration-distance profiles are discussed below.

3.5.1 Predictions from Simple Dispersion Modeling

²⁴ Beggs (2003)

²⁵ Van Riel et al (2007), Shinya et al (2006).

²⁶ Tang and Settles (2008)

The aerodynamic behaviour of a "cloud" of respiratory discharge is governed by the particulate properties of the droplets that make up the cloud, and therefore simple air emission dispersion modeling can be used to illustrate how droplet concentration per unit volume of air would be expected to diminish with increasing distance from the point of emission.

A cough or sneeze can be visualized as a three dimensional cone with an angle of about 90 degrees.

Assuming instantaneous discharge of the entire population of aerosol droplets comprising a sneeze (let's say 40,000 droplets), the concentration in a space immediately beneath the nostrils measuring 4 cm x 4 cm x 4 cm would be 625 droplets / cc. If we assume that this population of droplets then disperses outward with the N-S and E-W axes progressively enlarging to follow the cone, but the front-back axis stays 4 cm (which imagines the droplets moving forward together as a cluster), then we have a two dimensional droplet dispersion model. Under this model, the concentration drops progressively, such that at 20 cm the concentration is approximately 25 droplets / cc, at 40 cm - 6.25 droplets / cc, at 60 cm – 3 droplets / cc, at 1m – 1 droplet / cc, and at 2m – 0.25 droplets / cc.

The model can also be constructed using the assumption that the front-back axis remains fixed at the nostrils at one end, and the other end progressively and rapidly moves forward as the "sneeze front". This is a three dimensional droplet dispersion model. Using this assumption, the concentrations at the various distances are considerably lower than in the two dimensional model.

The expected geometric decline in concentration as a function of distance is the rationale for social distancing as a precautionary measure against respiratory infectious diseases.

3.5.2 Predictions from Ballistic Behaviour and Evaporation

The models described above also assume that the sizes of droplets in the respiratory aerosol are all the same (i.e. "monodispersed aerosol"). When the droplet cloud is comprised of droplets having a wide range of sizes, the droplets would not be expected to move forward together as a cluster, because their momentums will differ because of their different masses, as will their evaporation rates (and hence rate of reduction in size), and the rate at which their velocity is attenuated by fluid resistance of the air. For this reason, the concentrations at any given distance would actually be expected to be

considerably lower than predicted in Section 3.5.1, because of the progressive air attenuation of an increasing fraction of the particles as a function of distance.

Given that droplets of different aerodynamic diameters will travel different distances by ballistic movement, and that all droplets in the dispersion cloud are continuously evaporating as they move, the actual droplet concentrations at any point in space would be expected to differ from the concentrations predicted by simple dispersion modeling, and as a result, the virus concentrations may also differ. There may also be systematic differences in virus concentration profiles between sneezes, coughs, talking and simple exhalation, due to differences in the size range profiles of the droplets expelled by these different acts. One alternative dispersion scenario imagines the highest virus concentrations at the terminal ballistic travel distance for large particles. This is a plausible scenario if several conditions hold true.

First, the initial droplet size distribution would be weighted such that >95% of the droplet mass is represented by particles in the size range of 50 to 100 microns. This condition holds true for sneezes, but less so for coughs, talking, and exhaling.

Second, the largest particles travel the farthest before stopping, and are dispersed along a narrower angle than the overall population of droplets. The ballistic properties of particles predict this would be the case. Again, this would be a more significant factor for sneezes than other forms of respiratory aerosol discharge, due to the higher fraction of large particle diameters generated by sneezes.

Third, the distribution of viruses in the cloud would have to be proportionate to the size distribution profile of the droplets - in other words, the concentration of viruses in droplets would be the same regardless of droplet size. As noted earlier, it is not known whether this is the case.

If all three conditions hold true, then the largest particles that represent over 95% of the total liquid volume of a respiratory aerosol discharge would be delivered to and stop in mid-air about 60 cm from the point of discharge, and within a few seconds most will have evaporated in mid-air, leaving over 95% of the expelled viruses swirling around in a cloud approximately 60 cm from the emission source (assuming initial virus concentrations in all droplets are similar). Under this scenario, the highest concentration of droplet-free airborne viruses could be realized at about 60 cm from the face of the patient.

3.6 Relationship of Virus Exposure Concentration to Inhaled Dose

It is presumed that in the absence of respiratory protective equipment usage, an individual's inhaled dose of virions is proportional to the time-weighted average concentration of aerosols to which the person has been exposed.

3.7 Relationship of Inhaled Dose to Infection

The relationship between influenza virus inhaled dose to infection has not been well characterized, but a case report involving an outbreak amongst airline passengers noted a positive correlation between duration of potential exposure to respiratory aerosols and attack rates²⁷, and more recently a controlled experiment has demonstrated a dose-response effect for infection by rhinovirus²⁸. Both commonplace observations and the literature on influenza transmission note that risk of transmission increases in close proximity to an infected person, and this is plausibly a reflection of an airborne dose-response relationship.

A better understanding the relationship between total dose, dose intensity over time, and risk of infection is needed for respiratory protection strategies that are both rational and optimal. In particular, it would be important to know whether infection is caused mainly by an **acute point-in-time high level virus dose** (as may be hypothesized in respect of AGMPs), or whether **repeated low level exposures over a certain timeframe** can also cause infection (e.g. repeated exposure to coughs or sneezes, which is consistent with common experience). The range of individual susceptibilities to exposure would also be very useful information.

3.8 Non-Aerosol Respiratory Liquids and Solids²⁹

In addition to being expelled within aerosols, viruses may be expelled in respiratory liquids and solids in non-aerosol form. This includes liquid nasal discharge, nasal crusts, and saliva, all of which may be expelled spontaneously onto surfaces or other persons, or removed by the insertion of a finger or object into the nose or mouth by either the individual or another person (e.g. a HCW, parent, etc.).

Once transferred to skin, clothing or objects, laboratory and field research has determined that influenza viruses may remain viable for varying lengths of time (from minutes to days) depending on the chemical and physical properties of the surface upon

²⁷ Moser (1979)

²⁸ Bischoff (2009)

²⁹ The information in Section 3.8 is discussed at length by several sources: Boone (2007), Brankston et al (2007), Winther et al (2007), Weber et al (2008).

which they rest (pH, temperature, electric charge characteristics), and a variety of different environmental conditions (mainly temperature, humidity, and ultraviolet exposure).

Influenza viruses can be transferred between surfaces (including skin surfaces) by surface-to-surface contact. It is postulated that virus concentrations per unit of surface area could increase on commonly touched surfaces (e.g. door handles) during periods when those surfaces are repeatedly touched by (1) infected persons who have contaminated their own hands by covering their mouths or noses during a cough, or touching surfaces contaminated by droplet discharge; or (2) non-infected persons who have touched other contaminated surfaces. It is also possible that repeated touching of surfaces may remove viruses and reduce the virus concentration per unit of surface area if the number of "clean hands" that touch the surface exceeds the number of "dirty hands" that deposit contaminants.

"Contact transmission" theory postulates that the transfer of viable virus to the hands can lead to infection by self-inoculation to mucous membranes followed by translocation of the virus to the target respiratory tissues.

4.0 The Case “For” and “Against” Various Modes of Influenza Transmission

Experts’ beliefs about (a) whether influenza is transmitted in specific ways, and (b) the relative significance of those modes of transmission, influence their advice with respect to precautionary measures to minimize or prevent the spread of influenza. Therefore, in this Section we explain our understanding of the case “for” and “against” various modes of influenza transmission.

4.1 Infection by Non-Visible Particles in the Proximal Atmosphere

With reference to our model, infection by particles under 50 microns in the proximal atmosphere is postulated to occur via the following pathway: A1 to A3 (comprised of A31+ A32 + A33) to (A321 + A331).

The Case “For”

- It is conclusively established that influenza viruses are present in non-visible particles expelled from the respiratory tract of infected persons.
- There is considerable laboratory and field evidence showing that influenza viruses can be measured in air expelled from human subjects, patients, and animal subjects.
- There is considerable laboratory evidence showing that airborne influenza viruses can remain viable for significant periods of time while suspended in air, and that survival can be systematically altered by changing temperature and relative humidity conditions. There are no reasons to expect that airborne survival behaviour in commonplace indoor environments would be significantly different from survival behavior in laboratory atmospheres that simulate common indoor environments.
- The relationship between inhaled particle size and locus of deposition in the respiratory tract has been established and re-confirmed over the past fifty years.
- The locus of deposition of non-visible particles in the respiratory tract spatially corresponds to the locations of respiratory tissues that are well known by pathological observations and tissue culture studies to be infected by types and strains of influenza A.

- While it is the case that >95% of the liquid mass in a typical respiratory discharge is initially represented by visible particles, about 9/10ths of the droplets in the initial population are non-visible particles³⁰. In addition, most visible particles rapidly evaporate to form non-visible particles, meaning that essentially the entire population of particles produced by a respiratory discharge is inhalable within a few seconds of generation.
- There are logical reasons to believe that in the initial population of respiratory droplets produced by a discharge, non-visible respiratory droplets may contain significantly higher concentrations of influenza viruses than visible droplets. These are as follows: (1) non-visible droplets emanate from the deeper regions of the lungs³¹, and (2) those regions are likely to have more tissue infection (and hence more viruses in fluids on the epithelium) than the sinuses and pharynx.
- There are several published experiments involving different animal test systems where influenza was transmitted between infected and non-infected subjects sharing airspace but completely separated by sufficient distance to preclude the possibility of droplet or surface-to-surface transmission³². Manipulation of temperature and relative humidity conditions obtained results in terms of infection transmission rates that are consistent with laboratory experimental findings on the effects of temperature and humidity on virus survival in air.
- There are several anecdotal human case reports involving transmission where it appears that droplet or contact transmission was unlikely.
- Virtually all of the infection case reports in the literature where authors concluded transmission by "droplets" or contact could equally have been caused by exposure to non-visible particles in the proximal atmosphere. In no cases did researchers or clinicians actually exclude non-visible particle transmission as the mode, nor positively demonstrate droplet or contact transmission.
- There is evidence of proximal transmission by non-visible particles is accepted to occur for a variety of other viral, bacterial and fungal respiratory infections. In our view, the quantity and quality of that information is not clearly superior to the corpus of evidence in support of non-visible transmission of influenza in the proximal atmosphere.

³⁰ Morawaska et al (2009)

³¹ Morawaska et al (2009)

³² Tellier (2006), Weber et al (2008), Murbareka (2009), Munster (2009)

- There are a small number of case reports and case-control studies that show a protective effect from using N95 respirators (which trap visible and non-visible particles) as compared to use of non-rated "masks" (which are markedly less efficient in capture of visible particles, and essentially trap few or no non-visible particles), and use of no respiratory protection at all.
- There is one reasonably well-controlled experimental study report utilizing rhinovirus involving a small number of human volunteers which demonstrates the protective effect of using an N95 respirator versus masks or non respiratory protection. This same study also demonstrated a virus aerosol concentration dependent dose-response relationship for infection.
- Laboratory testing demonstrates that N95 respirators remove from the airstream a high percentage of non-visible aerosols down to the sub-micron size range, as well as the quantities of virus penetrating the mask.
- The proximal atmosphere non-visible particle mechanism is consistent with the empirical observation that most transmission is associated with "close contact" with an infected person.

The Case "Against" (And Weaknesses)

- Historically, most published influenza case reports (as well as initial reports on SARS) concluded that transmission was by "droplet" or "contact", as opposed to "airborne". *(In virtually every case the conclusion was simply a presumption, and not supported by positive evidence demonstrating that mode, or negative evidence discounting alternative modes).*
- In a sneeze, visible droplets typically constitute over 95% of the mass of the aerosol, and hence it is presumed that over 95% of the virus exposure is associated with these visible droplets. The amount of virus in the large droplets dwarfs the amount in the small droplets, despite the fact that the latter constitute typically 9/10ths of the droplet population. Therefore, contact with large droplets is more likely to cause illness than inhalation of small aerosols. *(The presumption of a direct positive correlation between particle size liquid mass distribution and virus mass distribution for sneezes has not been demonstrated and there is a logical counter-hypothesis (see Section 3.2.1). Also, all visible droplets almost instantly become significantly smaller non-visible droplets, so particle-size related differences in virus exposure may not occur in reality. Coughs have smaller particles and a particle size*

distribution that is less positively skewed than sneezes, and hence any large-droplet dosing effect would not be as significant for coughs.)

- If transmission occurs by non-visible particle exposure in the proximal atmosphere you would expect to see more nosocomial influenza amongst HCWs, but you don't - authors report that those cases that do occur appear to be related to exposure to visible droplets. *(There will always be a positive correlation between the concentration of visible droplets and the concentration of non-visible aerosols because the visible droplets so quickly evaporate to form non-visible aerosols. Where there are more visible droplets there will be higher exposure to non-visible particles both because of the likelihood of there generally being a correlation between the quantities of expelled visible and non-visible droplets, and the conversion of visibles to non-visibility.)*

4.2 Infection by Non-Visible Particles in the Distal Atmosphere

With reference to our model, infection by non-particles in the distal atmosphere is postulated to occur via the following pathway: A1 to A3 (as A31+A32+A33) to A322 to A3321.

The Case "For"

- The general case "for" infection by non-visible particles in the proximal atmosphere applies to the distal atmosphere. The key difference between the two scenarios is that the concentration of virus in the distal atmosphere would always be very significantly lower (by an order of magnitude of 10^4 and higher as compared with the proximal atmosphere).
- In a case report concerning an influenza outbreak at a US Veteran's Administration hospital in 1957 the authors reported a correlation during the course of a community outbreak between (i) the presence of UVGI lighting in parts of the facility and (ii) significantly lower rates of patient influenza as compared to parts of the facility without UVGI lighting. Since UV has been shown effective in deactivating influenza virus in air, it was postulated that the lower infection rates may have been due to the presence of UVGI. If UV was protective in the manner suggested, it would support the hypothesis that influenza can be contracted in the distal atmosphere by elevation of ambient airborne virus concentrations above some "background" level that is non-infectious, since the UVGI lighting only acted on the distal atmosphere³³.

³³ McLean (1961), Riley (1974), Tellier (2006)

- If there is some dose-response and duration of exposure-related proportionality for contracting influenza as a result of exposure to non-visible aerosols (as common experience suggests), and if the necessary dose can be acquired by exposure to respiratory aerosols discharged by a single sick person, then it is possible that in facilities with poor ventilation and large numbers of influenza cases the ambient virus concentration could reach levels comparable to those experienced when in close proximity to a single sick patient. This can be demonstrated mathematically. The relationship between adequacy of general ventilation and respiratory infection rates in hospital settings has also been demonstrated³⁴.
- It is common experience for persons to contract influenza without necessarily having been exposed to a person whom they know to have been infected or symptomatic. In past this has been presumed to be a consequence of surface-to-surface transfer of virus followed by self-inoculation, but it could equally plausibly be a consequence of exposure to elevated ambient concentrations of influenza virus.

The Case "Against"

- Dispersion modeling can be used to show that airborne virus concentrations rapidly drop to extremely low concentrations in large ventilated airspaces. If such low concentrations can cause infection, it is suspected that the associated infection rates are very low.
- In clinical settings there has not been any striking evidence that infection in the distal atmosphere occurs. (However, it is possible that cases presumed to be caused by surface-to-surface contact transmission could be cases of infection in the distal atmosphere.)

4.3 Infection by Visible Particles in the Proximal Atmosphere - Ballistic Introduction to Mucous Membranes

With reference to our model, infection by particles over 50 microns in the proximal atmosphere is postulated to occur via the following pathway: A1 to A2 to A21 to A214 to C4, and / or A1 to A2 to A22 to C4.

The Case "For"

³⁴ Beggs (2003)

- The case “for” this mode is largely the same as the case “against” Infection by Mucous Membrane Contact with Non-Visible Particles in the Proximal Atmosphere.

The Case “Against”

- Droplet transmission theory often focuses on entry of virus via the eye. The eye itself is not a site of influenza infection. This mode of transmission requires virus to be deposited onto the conjunctiva and then translocated down the lacrimal duct to the sinuses, and then either (a) inhaled into the lungs inside droplets generated within the sinuses during inspiration, or (b) translocated to target tissues in the lungs by other as of yet non-delineated mechanisms. There is no evidence that (a) or (b) occur, nor have any plausible translocation mechanisms been postulated.
- Visible particles that are inhalable will be deposited in the nostrils or sinuses (this is well established). This mode of transmission requires viruses deposited in the nose or sinuses to be either (a) inhaled into the lungs inside droplets generated within the sinuses during inspiration, or (b) translocated to target tissues in the lungs by other as of yet non-delineated mechanisms. There is no evidence that (a) or (b) occur, nor have any plausible translocation mechanisms been postulated.
- There is no experimental or clinical evidence indicating that putting one's fingers in the mouth can increase risk of contracting influenza.
- Ballistic movement of visible particles terminates in air at about 60 cm from the point of emission. Therefore, droplet transmission should only occur in very close proximity to the breathing zone of the patient, but clinical reports suggest that this degree of closeness is not necessary for infection to be transmitted from person-to-person.
- There are no animal studies demonstrating translocation of virus from the eye to the lungs. There are studies whereby virus was introduced into the eyes of animal test subjects are resulted in low rates of infection, but in these studies the method did not preclude entry of the inoculant into the nose of the test animal.
- In a recently reported controlled experiment utilizing rhinovirus and a small number of subjects, researchers found that selective exposure of the conjunctiva to rhinovirus aerosols of differing concentrations did not induce infection of the eye or the respiratory tract³⁵.

³⁵ Bischoff (2009)

4.4 Infection by Deposit of Visible Particles to Surfaces followed by Mucous Membrane Self-Inoculation

With reference to our model, infection by particles over 50 microns in the proximal atmosphere is postulated to occur via the following pathway: A1 to A2 to A21 to A211, A212, A212 to several possible points in the "Contact Zone", and finally via C3 to C4, or C14 to C15.

The Case "For"

- Influenza viruses can remain viable for varying amounts of time on different surfaces and under a range of environmental conditions, and hence be available for uptake by contact with those surfaces.
- Viruses can be transferred between surfaces, including to and from skin surfaces.
- Viruses on fingers and hands can be self-inoculated into the eyes, nose and mouth.
- Self-inoculation by children has been found to be associated with increase rates of upper respiratory infections (although not influenza specifically).
- Hand-hygiene practices have been found in a few studies to have a mild protective effect for upper respiratory infections.
- It is well established that in health care settings that rates of many types of infections (non-influenza upper respiratory, gastro-intestinal, and opportunistic) are reduced by disinfecting surfaces and higher compliance with hand hygiene protocols.

The Case "Against"

- In every published infection case report where the author(s) concluded influenza transmission by "contact", transmission could equally have been caused by exposure to non-visible particles in the proximal atmosphere (the relative contributions of different modes were not assessed, nor were modes of transmission controlled).
- Ballistic movement of visible particles terminates in the air at about 60 cm from the point of emission. Therefore, contact transmission of this manner should occur primarily as a result of contact with surfaces that are readily or repeatedly

contaminated as a result of their being in close proximity to the infected person (such as telephones, keyboards, personal effects, etc.).

- There are no animal studies demonstrating this mode of transmission to the exclusion of other modes.
- Hand-hygiene practices have been found in a few studies to have only a mild protective effect, and in other studies to have no protective effect. Protective effects have also been limited to either (a) upper respiratory infections, or (b) "respiratory infections" generally (not specific to influenza), and / or (b) other non-influenza infections. There are no studies demonstrating a specific protective benefit in relation to influenza.

4.5 Infection by Deposit of Non-Aerosol Respiratory Liquids or Solids to Surfaces followed by Mucous Membrane Self-Inoculation

With reference to our model, infection by virus-contaminated respiratory liquids and solids is postulated to occur via the following pathway: N1 to anywhere in the "Contact Zone", then C3 to C4, or C14 to C15.

The Case "For"

- The case "for" this mode is largely the same as the case "against" Infection by Deposit of Visible Particles to Surfaces followed by Mucous Membrane Self-Inoculation.

The Case "Against"

- Virtually all of the infection case reports in the literature where authors concluded transmission by contact could equally have been caused by exposure to non-visible particles in the proximal atmosphere.
- There are no animal studies demonstrating this mode of transmission.
- There are no human studies demonstrating this mode of transmission.
- Hand-hygiene practices have been found in a few studies to have only a mild protective effect, and in other studies to have no protective effect. Protective effects have also been limited to either (a) upper respiratory infections, or (b) "respiratory infections" generally (not specific to influenza), and / or (b) other non-influenza

infections. There are no studies demonstrating a specific protective benefit in relation to influenza.

5.0 Implications of the Cases “For” and “Against” for Respiratory Protection Usage by Health Care Workers

We consider the implications of the information presented in Section 3.0 and 4.0 to be as follows:

1. While not proven conclusively (e.g. through controlled experiments on humans), there is now a considerable body of evidence, from various lines of viral aerosol transmission and survival research, animal experiments, and case reports, to suggest that inhalation of non-visible aerosols containing influenza virus (i.e. **exposure**) can cause disease transmission.
2. Diligent use of well-fitting NIOSH-approved high efficiency particulate aerosol filtering respirators (e.g. N95) when providing care within a 2 meter zone of an influenza patient will result in significantly reduced **exposures** to respiratory aerosols, in comparison with using no respiratory protection at all, or using only surgical or procedure masks.
3. Reducing inhalation exposure to respiratory aerosols should reduce incremental risks of contracting influenza in providing patient care in the proximal atmosphere.
4. Measures that are effective in reducing or containing respiratory aerosol discharges from patients are likely to reduce HWC worker exposures to respiratory aerosols, and may thereby reduce risk of patient-to-HCW transmission of influenza. This includes conventional practice of cough and sneeze etiquette by the patient, as well as containment of discharges by use of surgical or procedure masks.
5. Transmission of influenza via droplet impact on the conjunctiva is not likely to be a significant mode of transmission. Consequently eye protection and face shields are unlikely to reduce person-to-person transmission of influenza.

6.0 Comments on the PHAC Document

The following comments are made within the context of information presented in Sections 2.0 through 5.0 of our paper.

We begin with comments on several content items in the body of the document that we consider to be significant misstatements of fact, or non-substantiated statements presented in a manner that may create the impression that they are authoritative. We then identify several points that we consider to be ambiguous and in need of further explanation. We also comment on what appears to be a double standard of proof that PHAC applies in respect of aerosol transmission versus other modes. Finally, we comment on the four control levels model that we understand to be a deterministic outcome for point-of-care risk assessment, conducted in the manner recommended by PHAC. In this latter context we also discuss concepts of point-in-time versus cumulative aerosol exposure, which may be relevant to risk of infection but receives no coverage in the PHAC document.

6.1 Significant Misstatements and Non-Substantiated Statements

Influenza Receptors in the Upper Airway

- Lines 700-701: "Roy 2004" which is cited as authority for the statement "that influenza viruses...are deposited on viral receptors in the upper respiratory tract". No specific citation is provided apart from "Roy 2004". We were unable to locate any relevant citation authored by any "Roy" published in 2004 that contained information consistent with this assertion. An article entitled "Airborne Transmission of Communicable Infection – The Elusive Pathway", by Roy CJ et al (2004), is the only article that we identified that addresses the general subject area of respiratory disease transmission, and this article does not contain any content relating to viral receptors or their locations in the human airway.
- Lines 701-702: "Shu-An Lees, Am Occup Hyg Vol 52 2008" is cited as authority for statement "Receptors for human influenza virus are primarily located on the nasopharyngeal mucosa". No such statement is made in this article. The referenced citation reports on the efficacy of N95 respirators, and does not address the distribution of influenza virus receptors in the airway.
- These statements are inconsistent with well established knowledge on the pathology of many types of influenza infections, which are predominantly infections of the epithelium of the bronchioles and trachea, sometimes accompanied by complicating infection of the alveoli. According to Kuiken et al (2008),

“Uncomplicated human influenza virus infection causes transient tracheo-bronchitis, corresponding with predominant virus attachment to tracheal and bronchial epithelial cells.”

Authority for Contact, Droplet and Aerosol Transmission

- Lines 735-739: There is no authority or evidence cited for the statement "Pandemic influenza contact transmission may occur when contact exposure leads to an infectious dose of viable pandemic influenza particles from an infected/contaminated source being inoculated onto mucous membranes, (i.e., eyes, nose and mouth) contiguous with respiratory virus receptors in the host's upper airway and overcome other host defenses". PHAC does not acknowledge the evidentiary, logical or physiological weaknesses of this postulated modality, nor present opposing empirical evidence.
- Lines 754-761: There is no authority cited for the statement "Pandemic influenza droplet transmission may occur when the droplets that contain an infectious dose of viable pandemic influenza particles are propelled a short distance (less than 2 meters) through the air and come into contact with influenza virus receptors in the host's upper airway and overcome other host defenses". PHAC does not acknowledge the evidentiary, logical, physical or physiological weaknesses of this postulated modality, nor present opposing empirical evidence.

AGMPs Generate Smaller Infectious Droplets than Spontaneous Discharges by Patients

- Lines 748-749: "Fowler 2004" and "Lee 2003" are cited as authority for the statement "AGMPs may result in the generation of smaller infectious droplets, which can travel further than those generated spontaneously from patients." The work reported on in Fowler's and Lee's publications did not involve measurement of the size distribution or quantities of aerosols associated with AGMPs. Fowler and Lee were simply expressing opinions, which were not substantiated by any evidence or logical rationale. The assertion that "smaller infectious droplets... can travel further than those generated spontaneously from patients" is not consistent with what is known about the ballistic and aerodynamic behaviour of droplets. There is also no evidence that we have found to demonstrate that AGMPs generate smaller infectious droplets than voluntary aerosol discharges.

Size Threshold for Large Particles that Quickly Fallout from Air

- Lines 855-856: "Large particles (>10 microns) will fall quickly (in a few seconds) to the ground and are considered to represent a droplet exposure" (Roy 2004)." This is not correct. A 10 micron particle with unit density has a terminal settling velocity in air of 0.003 m/s, which means it would take about 5 minutes for that particle to drop 1 meter, in perfectly still non-convective air. However, a droplet of this size would convert to a droplet nucleus within a few seconds, meaning that it would never actually fall to the ground.

Evidence for Translocation of Infectious Virus Aerosols Beyond 2 Meters

- Line 861-863: "To date there is little evidence to suggest that viable infectious influenza virus particles are carried measurable distances beyond the room or two meter bed space". PHAC fails to mention that a high fraction of viruses contained in respiratory discharge will remain suspended in air, and that there is considerable evidence that airborne influenza virus will survive for several minutes or hours depending on conditions, and that suspended virus particulate will be dispersed and distributed by passive air movement and ventilation systems. This information, combined with fairly basic understanding of mechanical ventilation system operation, airflow dynamics, and the law of mass conservation, leads to the conclusion that viable infectious influenza virus particles will indeed be carried measurable distances from their source.
- PHAC is confusing the translocation of suspended virus particles with the question of whether the resultant concentration and exposures in distal atmospheres are sufficient to induce infection.

Omission of Review Articles on Mode of Influenza Transmission

- PHAC doesn't include Weber (2008), or Tillier (2006), or Bridges (2003) in its list of recent "systematic reviews on the transmission and control of seasonal influenza". Weber, Tillier and Bridges all conclude that transmission by non-visible droplets in the proximal atmosphere may be important modes of transmission in both community and health care settings.
- PHAC suggests that conclusions made by "Brankston et al (2007)" and "Jefferson et al (2009)" support PHAC's assertion that droplet and contact transmission are the predominant routes and that "airborne" (which PHAC fails to define in relation to these articles) is neither the predominant mode nor frequent enough to worry about. This is not an accurate characterization:

- The Jefferson article, which is mis-cited as 2009, but is 2007, was a review of research reports on a variety of different upper and lower respiratory infections. The studies they looked at didn't specifically focus on influenza, and the control measures studied weren't specifically in relation to influenza. The hygiene interventions appeared to be effective for upper respiratory infections (colds), but the authors report that a broad range of preventive interventions have shown inconsistent levels of effectiveness across different studies.
- Brankston et al do not in fact state what PHAC claims they state. In addition, Brankston et al consider "airborne" transmission to mean transmission at long distances, not close distances. Moreover, in relation to "droplet" transmission it is important to note that they define the "droplets" associated with droplet transmission to be 5 microns and larger - but these are in fact non-visible particulates, not the visible "droplets" conventionally referred to in relation to droplet transmission. These issues are discussed in detail under Section 7.3 herein in relation to the use of Brankston et al in the SHEA position paper, and the comments made there are equally applicable to the use of Brankston et al in the PHAC.

The Assumption of No Incremental Risk for HCWs in Healthcare Settings

- Line 966: PHAC states "During an influenza pandemic, there will be risk of transmission of influenza in all community settings. When patients, HCWs, other staff, visitors, contractors, etc. are in the larger community (e.g., at home, at school, shopping) they will share the same risk of acquiring influenza as the general population and be at no increased risk while working in any healthcare setting" (underline added). Given that during a pandemic HCWs will have more frequent and longer duration contact with influenza cases than anyone else, it is inconceivable that HCWs would not face increased risk of contracting influenza in relation to non-HCWs. PHAC offers no explanation of the basis for its assertion.
- It is possible that comments in the PHAC paper with respect to incremental risk reflect a current perception that HCWs have not been found to have rates of H1N1 illness that are higher than the rate in the general population. However, this is only our assumption since the PHAC paper does not explicitly state this as the basis for the assertion that there is no incremental risk. If the PHAC paper does intend to take the position that HCWs face no incremental risk from H1N1, PHAC should present data demonstrating that this has been the case since the commencement of the

outbreak in spring 2009 to present. Should such data exist, in our view it would not be sufficient at this time to demonstrate the absence of incremental risk for HCWs for the following reasons: (a) the actual incidence rate and total number of cases in Canada continues to be low, and therefore it is unlikely that a higher incidence rate amongst HCWs would be discernable unless there were obvious and frequent instances of occupational transmission (as was the case with SARS), and (b) the overall population incidence rate in Canada at present is not a reasonable statistic against which HCW incidence should be gauged, due to (i) the population age distribution for HCWs being different from that of the general population, and (ii) the elevated incidence rate observed in certain sub-groups within the general population.

The Need for Fit Testing

- Line 1240 - the assertion that fit testing is necessary to afford adequate protection when using an N95 is not substantiated, and there is evidence to the contrary. In our experience the assertion that fit testing is necessary is often used as an excuse for not recommending respirators in environments where fit testing is impractical or logistically non-achievable.
- A recent presentation at the Institute of Medicine workshop in August 2009 by Brosseau (2009) noted that the literature suggests that fit testing is not strictly necessary for N95 respirators to afford protective benefits.
- There are also significant differences between qualitative and quantitative fit testing, yet PHAC does not acknowledge these two variants, nor take a position on whether qualitative fit testing is acceptable.

Advice Against Use of a Powered Air Purifying Respirator (PAPR)

- Lines 1380 – 1386: PHAC states "Influenza is droplet spread [again, no authority has been cited], resulting in gross contamination of environmental surfaces within two meters of an infected source [again, no evidence or authority has been cited]. If a PAPR is worn for care (e.g. AGMPs) of a patient with symptoms compatible with influenza, the level of contamination of the PAPR surfaces [an unsubstantiated assertion] combined with the process for removing a PAPR will put any HCW wearing a PAPR for care of a patient with the influenza at risk of exposure to that influenza strain [again no evidence is cited in support of these assertions]." ***If this indeed will happen and is a risk, why would it not also happen if a HCW wears a mask or disposable N95 respirator?*** PHAC does not address this logical inconsistency. PHAC also fails to acknowledge the fact that PAPRs have been

routinely and safely used for high toxic, biological, and radioactive materials hazards for decades, and that there are well established and protective decontamination protocols.

- Lines 1387 – 1390: PHAC states "If a HCW or other staff cannot be fit tested for a respirator (e.g. facial disfigurement/deformity, HCW has a beard for religious reasons), consider limiting this HCW or other staff from performing AGMPs on patients with pandemic influenza." A positive pressure hooded respirator would be an acceptable alternative in these circumstances, but it is not mentioned. Also, PHAC fails to address the obvious question of whether this also means that those personnel who can't be fit tested for a respirator can still wear a "mask" (despite, presumably the existence of the same fitting issues with a mask).

6.2 Ambiguities

Gowns Always Required within 2 meters

- Lines 1422-1425: PHAC states "Gowns are not required for the routine care of patients with influenza or symptoms compatible with influenza, unless contact with clothing or skin of the patient, or contact with the patient's immediate environment (i.e. within 2 meters) is anticipated." When would "routine care" not result in entry into the 2 meter zone around the patient? Why not just say "gowns must be worn within 2 meters".

Meaning of "Special Handling"

- Lines 1449-1454: What is meant by "special handling"? Given the other advice re surface sanitization and hand washing, why would there no need for "special handling" of influenza patients' wastes, dishes, and secretion-contaminated linens?

Meaning of "Re-Use"

- Lines 1489-1490: What is meant by "re-use" in the context of disposable PPE? Particularly N95s and masks.

6.3 Double Standard

PHAC applies very different standards of proof in drawing conclusions with respect to various putative modes of transmission. The three mode-of-transmission review articles cited by PHAC, and the three additional mode of transmission review articles that we

have identified (Weber, Tellier, Bridges) reference 419 different peer reviewed scientific articles. Approximately 150 of these articles provide information that supports the case for non-visible aerosol transmission in the proximal atmosphere. These articles include case reports, laboratory experiments, and field evaluations. While many of the cited articles assert that droplet and contact transmission are the predominant modes of influenza transmission, or were responsible for the cases described in the article, not one of the articles actually demonstrates either mode to the exclusion of others, and none of the articles report on controlled experiments designed to demonstrate droplet or contact transmission in animal systems.

PHAC has not articulated the criteria that it uses to evaluate the quality of any particular information published in a scientific article, nor explained how it weights conflicting and coherent information, nor does it comment on its appraisal of the quality or importance of any of the research that it cites in the document.

6.4 Point of Care Risk Assessment

The Outcome in Decision Table 4 Doesn't Reflect Consideration of Most of the Influenza Exposure Risk Factors Identified by PHAC at Line 1708

The information provided in the table at line 1708 is very good, however most of these factors are not incorporated into the four table model. Line 1710-1729 indicates that a range of infectious agent, infected source, environmental features, and host features must be considered when practicing PCRA, however the four tables take a more simplistic approach that actually considers only one factor – that being whether an AGMP is being performed.

Based on information contained in the PHAC document, it would seem reasonable that Level IV controls would be utilized wherever "higher transmission risk" factors were present and the HCW had to enter the patient's room or otherwise be within 2m of the patient. However, the four table model does not lead to this conclusion.

The PHAC Model Does Not Consider Certain Key Factors Affecting HCW Exposure

In a health care setting the droplet exposure experienced by a HCW will increase as a function of the number of patient care interactions, the duration of time in close proximity to patients (e.g. length of the daily work shift and the work week), and the patient occupant density at the workplace. None of these factors influence the protective measures as determined by the four table model. ***Consequently, using the PHAC decision logic, a nurse having dozens of daily close contact patient care***

encounters 5 days a week with a ward full of influenza patients would be deemed by PHAC not to need an N95 respirator, but a physician performing a bronchoscopy an average of once per week would need an N95 respirator when performing that procedure.

The PHAC recommendations reflect no conceptualization of the impact of exposure frequency and duration on risk of infection. The recommendation for N95 use during AGMPs reflects the presumption that that patient to HCW transmission can or is most likely to occur as a result of short duration exposure to very high aerosol concentrations (assuming, of course, that high aerosol concentrations are associated with AGMPs, which has not been shown to be the case).

At present, the relationship between duration of exposure and airborne virus concentration has not been elucidated. It is therefore possible that transmission may occur as a result of short-duration high concentration exposures, and / or as a result of longer duration exposures at lower concentrations.

Criteria for Use of a Mask

No evidence is cited for the adequacy of recommendations concerning usage of face masks. Presentations made at the recent Institute of Medicine workshop in Washington D.C. August 11-13 provide a good synopsis of the evidence with respect to the inferiority of surgical masks for protection against respiratory aerosols³⁶. The logical rationale is also not apparent.

Under the first Level III scenario, if a patient is compliant with the requirement to wear a mask or uses tissues, and strongly coughs or sneezes in proximity to the HCW, does Level III assume that the controls utilized by the patient ensure that the HCWs exposure to visible and non-visible droplets is sufficiently such that low to be non-infective? Alternatively is it assumed that the level of filtration / attenuation provided by a mask is sufficient to render such exposures negligible? Or is it assumed that in this scenario, there is no inhalation exposure risk but only direct droplet impact exposure risk? No evidence is presented in support of any of these alternatives.

With respect to the second Level III scenario, is the assumption being made that a weak or absent cough means that the patient does not expel large or small aerosols, or is it that the HCW's mask provides adequate attenuation to render such exposures inconsequential, or is it that the quantity of aerosols discharged is sufficiently low that it

³⁶ See the Brosseau and Borwegan presentations.

presents no risk to the HCW? Moreover, how could it be asserted that a surgical mask affords adequate protection unless the filtration and protection factor requirements for such masks are specified?

6.5 Control Levels Concept in the Point of Care Risk Assessment Framework

6.5.1 Level I

Description

Level I controls are applied in two situations: (1) "non-patient, non-clinical" settings where the patient has no access to the HCW, and (2) settings where the HCW has "no direct interaction and no indirect contact" with any patients. Level I controls consist of hand hygiene and respiratory hygiene.

Analysis

The presumed purpose for hand hygiene is to minimize the potential for accumulation on the HCW's hands of influenza virus that may have been deposited on surfaces by other non-ILI cases who have had contact with ILI cases. Hand hygiene acts only on variable N1, and transmission pathways C1 to C2, and C11 to C13 shown in our model. Since it is presumed that there is no contact with ILI patients, and since there is in any event surprisingly little evidence that influenza is spread by contact transmission, the principal benefit of hand hygiene is likely to be reduction in risk of illness from other microbial diseases for which self-inoculation to mucous membranes is a more credible mode of transmission.

Respiratory hygiene acts mainly on variable A2, and transmission pathways A21 to A211, A212, A213, A214 shown in our model. PHAC uses the term "respiratory hygiene" to refer to containing a sneeze or cough with a sleeve, tissues or hands, and by wearing a procedure mask. All of these techniques differ in their efficiency and reliability. Since the HCW has no contact with ILI patients in the Level I scenario, it is presumably the HCW who is the focus for, and required to practice respiratory hygiene, presumably for the benefit of co-workers and others. It is not clear whether HCWs are expected to wear masks if they themselves are coughing or sneezing.

Practicing respiratory hygiene by the HCW may reduce the risk of transmission between an infected but asymptomatic HWC and a non-infected HCW, or from HCWs to non-infected or asymptomatic patients.

6.5.2 Level II

Description

Level II controls are applied in two different circumstances: (1) any manner of direct or indirect contact with any patient who has recovered from influenza (including AGMPs), and (2) any manner of indirect contact with any influenza patient (including contact with contaminated objects, and indirect contact in environments where AGMPs were performed).

Level II controls are essentially identical to Level I controls. The only difference between Level I and Level II is that an N95 respirator is to be used by the HCW if there is "known or suspected or active tuberculosis", and gloves and gowns are to be worn "as per routine practices".

Analysis

The comments under Analysis of Level I apply to Level II. With respect to the additional requirement for use of an N95 respirator for protection against the specified diseases, it is not clear when and where such respirators are to be used.

PHACs "Guidelines for Preventing the Transmission of Tuberculosis in Canadian Health Care Facilities and Other Institutional Settings (CCDR Vol 22S1 April 1996) stipulates "mask" or N95 use when: (a) caring for a patient with suspected or confirmed infectious TB; (b) entering a room where a patient with suspected or confirmed infectious TB is being isolated; (c) a patient with suspected or confirmed infectious TB is undergoing a procedure that is likely to produce aerosolized infectious particles or to result in coughing or copious sputum production, even if appropriate ventilation is in place; (d) in contact with a patient with signs and symptoms that suggest infectious TB; (e) manipulating mycobacterial cultures in the laboratory; or (f) performing an autopsy.

If a PCRA were performed in advance of any of the activities described in (a) through (d), it would not lead to the conclusion that Level II controls were applicable. Therefore, presumably the N95 respirator recommendation would only apply when performing activities such as those described in (e) and (f).

With respect to the use of gloves and gowns in Level II, it would appear that these would be required only in situations where there is contact with contaminated objects or entry into a room where an AGMP was performed on a patient who is no longer in the room. It is not evident that the use of gloves and gowns in these circumstances would reduce

risk of transmission of influenza. Level II does not appear to provide any incremental protection over Level I.

6.5.3 Level III

Description

Level III controls are applied when the HCW has any kind of direct interaction (except for AGMPs) with any influenza patient, regardless of the condition of the patient. The only difference between Level III and Level II is that eye protection and a procedure/surgical mask are also worn.

Analysis

Direct interaction with influenza patients presents potential for HCW exposure in the proximal atmosphere to both visible and non-visible respiratory aerosols, and bulk respiratory liquids and solids containing influenza virus.

All of the prior comments with respect to the elements in Level I and II apply to Level III.

The addition of eye protection is presumed to be to provide protection against the postulated mode of infection whereby ballistic impact of droplets on the conjunctiva creates risk of infection as a result of translocation to the respiratory tract. Therefore, eye protection acts on element A21 and pathway A21 to A214 shown in our mode.

The addition of a non-rated mask is presumed to provide droplet impact protection for the mouth, nostril area, and the facial skin covered by the mask. Therefore, the mask acts on element A21, and pathway A21 to A213, A214.

Level III controls do not provide any protection for HCWs against inhalation of non-visible respiratory aerosols, and provide only a small amount of protection against inhalation of visible respiratory aerosols. Since visible respiratory aerosols rapidly evaporate to form non-visible aerosols, Level III provides essentially no protection against respiratory aerosols or airborne influenza virus.

The inferences to be drawn from the Level III control recommendation are as follows:

- PHAC does not consider influenza to be transmitted by inhalation of respiratory aerosols containing influenza virus, and / or
- PHAC does not consider the quantities of such aerosols emitted by sneezing, coughing, talking or exhalation to be sufficient to cause infection - under any

- circumstances (except AGMPs), or combinations of exposure frequencies and durations - to cause an incremental increase in HCW risk of infection (i.e. higher rates than would result from community acquired influenza), and / or
- PHAC presumes that most of the total quantum of virus emitted in respiratory aerosols is carried within large droplets, and that a mask provides adequate attenuation of those droplets, and / or
 - PHAC accepts the possibility of an increased risk of infection amongst HCWs, but considers that level of risk to be acceptable (and presumably low) for reasons that PHAC has not articulated in the document.

6.5.4 Level IV

Description

Level IV controls are applied when the HCW performs, assists with, or enters the room during performance of an aerosol generating medical procedure. The only difference between Level III and Level IV is that an N95 respirator is used in Level IV versus a non-rated mask in Level III.

Analysis

The inference to be drawn from the Level IV control recommendation is that PHAC considers the degree of potential HCW inhalation exposure to infectious aerosols in association with AGMPs to be sufficient to cause increased risk of contracting influenza.

Concern regarding increased risk is supported by several case reports of HWC nosocomial infections with SARS or TB which occurred after performance or assistance with an AGMP, findings of increased relative risks amongst HCW sub-groups performing AGMPs, and clinical observations that some kinds and methods of AGMPs produce visible droplets during parts of the procedure.

The occurrence of these cases, particularly when they occur as small clusters, is suggestive of there being respiratory disease transmission risk associated with AGMPs, but it does not show that these procedures present in themselves a significantly higher risk than more routine exposures to voluntary aerosol discharges, nor that AGMPs account for the majority of HCW nosocomial respiratory infections.

Moreover, there are relatively few such published case reports, and many such procedures performed (in the USA alone there are estimated to be approximately

300,000 bronchoscopies annually - source: www.surgery.com) which may mean that AGMPs typically do not result in HCWs contracting infection.

If N95s are required for AGMPs but not other types of aerosol exposures, it implies that potential inhalation exposures from aerosol concentrations produced by a variety of AGMPs would:

- be significantly higher than,
 - point-in-time inhalation exposures experienced by a HCW either as a result of proximal exposure to a patient's sneeze or cough, and also
 - the total exposure experienced by a HCW over one or many work shifts, as a result of multiple contacts with influenza patients and entry into rooms of influenza patients, or that
- the risk of contracting infection from a brief high concentration exposure to viral aerosols is significantly greater than the risk associated with multiple lower concentration exposures, even when experienced repeatedly and over a prolonged period of time.

Both of these possibilities deserve consideration.

With respect to the first, there are no published reports that quantify the range of aerosol concentrations associated with AGMPs, or compare the relative contribution of AGMPs and other events (e.g. cumulative exposure to sneezes or coughs) to a HCWs overall exposure to potentially infective aerosols.

Davies et al (2009) reviewed the literature on production of aerosols by AGMPs and HCW risk of contracting illness in connection with AGMPs and concluded as follows:

"While there is compelling evidence that procedures such as bronchoscopies generate aerosols, the potential for aerosol generation from some procedures may have been overstated. Clearly, nosocomial transmission from patients to HCWs has taken place, but whether it is the AGP that is the primary source is difficult to clarify. Without further quantitative research to establish definitively the presence/absence of aerosols from these procedures it will be difficult to lay to rest the uncertainty that surrounds these procedures. Where there is uncertainty, there is a greater concern for the clinicians who will have to make decisions during the next outbreak of a respiratory disease, With a subsequent impact on human and material resources, until definitive evidence is generated, appropriate RPE training and fit testing should be given to HCWs to deal with the worst case scenario."

A simple mathematical exercise can be used to illustrate the amount of aerosol droplet exposure from a AGMP that would be required to equal the exposure associated with being sneezed upon by a patient. A sneeze reportedly may contain 40,000 aerosol droplets, which is considerably larger than the numbers associated with coughs, talking or exhalation. Since Level III does not require N95 respiratory protection, we presume that exposure to air into which 40,000 droplets have been expelled is considered "safe", even if the HCW is exposed in close proximity to the patient. To translate this into an exposure concentration parameter, it is necessary to make an assumption with respect to the dispersal of those droplets in a volume of air. For simplicity we can assume the sneeze disperses uniformly into a 90 degree conical volume that extends approximately 1 meter from the point of discharge. This produces a volume of approximately 0.5 cubic meters, resulting in a maximum transient concentration of 80,000 per cubic meter. Hence, for sake of the illustration, we can consider 80,000 droplets per cubic meter as a "safe" maximum transient concentration for droplets. This "safe" concentration would then be the maximum transient concentration permissible inside the N95 mask worn by a HCW performing an AGMP. If we assume, for simplicity, that 95% of all droplets are filtered out by the N95 mask, then the maximum transient concentration permissible outside of the mask (i.e. in the same 90 degree conical volume extending 1 meter from the patient's breathing zone) is $80,000 \times (95/5) = 1,520,000$. Therefore, by requiring N95 respirators for AGMPs but not for sneeze protection, the assumption is being made that the ambient concentration near the patient's breathing zone during an AGMP may be significantly higher than 1.5 million droplets per cubic meter, and hence present increased risk.

With respect to the second possibility, it is not known whether the risk of contracting infection from a brief high concentration exposure to viral aerosols is significantly greater than the risk associated with multiple lower concentration exposures, even when experienced repeatedly and over a prolonged period of time. Hall et al (1979) report that for some viral diseases the amount of viral dispersal correlates with the severity of infection, but the relative effects of the magnitude of the virus concentration to which one is exposed, the duration of exposure, and the effects of cumulative exposure have not been studied.

7.0 Comments on the SHEA Document

It is our understanding that HSABC and NUPGE are specifically concerned with the following SHEA recommendation:

“...we recommend the use of surgical masks for respiratory protection during routine patient care activities as opposed to continued universal use of N95 particulate respirators.” (Page 3, Paragraph 2)

We offer the following comments on this recommendation, within the context of information presented in Sections 2.0 through 5.0 of our paper.

7.1 Apparent Basis for the SHEA Position

The SHEA position on use of surgical masks versus N95 respirators appears to be based upon the following assertions:

1. Both H1N1 and seasonal influenza are spread by large respiratory droplets.³⁷
2. Evidence for airborne transmission of seasonal influenza is lacking...” (SHEA, Page 1 Paragraph 3).
3. In view of (1) and (2), N95 respirators provide no higher level of protection over surgical masks.³⁸
4. Routine use of N95 respirators for H1N1 patient care could deplete supplies, which in turn could preclude N95 usage by healthcare workers in circumstances where the need for N95 respirators is more clearly established (e.g. care of tuberculosis patients).

We address each assertion below.

7.2 Spread by Large Respiratory Droplets

SHEA does not define what it means by “large respiratory droplets”, and cites no authority for this assertion. Also, as noted in Section 3.3 herein, visible droplets rapidly convert to non-visible droplets. The state of knowledge with respect to modes of transmission is discussed at length in Sections 3, 4 and 6 above.

7.3 Evidence for Airborne Transmission of Seasonal Influenza is Lacking

SHEA cites the following three publications as authority for this statement:

³⁷ “Seasonal influenza is spread by large respiratory droplets” (SHEA, Page 1, Paragraph 3).

“Consistent with current scientific knowledge concerning the dynamics of transmission of seasonal influenza, available data and clinical experiences suggest that novel H1N1 transmission also occurs, like seasonal influenza, via droplet spread.” (SHEA Page 2, Paragraph 1)

³⁸ “Inappropriate and widespread use of N95 respirators for all novel H1N1 patient care activities does not provide increased protection against the virus and may have an adverse impact on patient and healthcare worker safety.” (SHEA Page 3, Paragraph 2)

Lemieux C, Brankston G, Gitterman L, Hirji Z, Gardam M. Questioning aerosol transmission of influenza. *Emerg Infect Dis* 2007; 13: 173-4; author reply 174-5.

Bridges CB, Kuehnert MJ, Hall CB. Transmission of influenza: implications for control in health care settings. *Clin Infect Dis* 2003; 37: 1094-101.

Brankston G, Gitterman L, Hirji Z, Lemieux C, Gardam M. Transmission of influenza A in human beings. *Lancet Infect Dis* 2007; 7:257-65.

In fact, none of these publications provide authority for SHEA's position. SHEA has also failed to cite two review articles where the authors reached the opposite conclusion (Tellier 2006, Weber 2008).

Lemieux et al

The Lemieux et al citation is in fact a letter to the editor in which the authors oppose the conclusions made by Tellier (2006)³⁹ with respect to the occurrence and potential significance of aerosol transmission. Lemieux et al take issue with the interpretation of the findings of specific research reports cited by Tellier. Our understanding of Lemieux et al's letter is that they believe that methodological or conceptual limitations associated with specific pieces of cited research preclude Tellier from drawing the conclusions he does with respect to the likely significance of influenza transmission by inhalation of respiratory aerosols. Tellier's paper reviews a variety of types of evidence, and limitations associated with individual studies are not unexpected. In the same issue as Lemieux et al, Tellier also responds to their specific comments.

With respect to SHEA's use of the Lemieux et al citation, we offer the following comments. The Lemieux et al citation is not a peer reviewed paper, it is a letter to the editor. SHEA treats the letter as an authority for SHEA's assertion that "evidence for airborne transmission of seasonal influenza is lacking". SHEA also elects not to cite Tellier's rebuttal, nor Tellier's original peer reviewed article, which reaches conclusions contrary to SHEA's position.

Bridges et al

³⁹ Tellier, R. A Review of Aerosol Transmission of Influenza A Virus. *Emerg Infect Dis* 2006; 12: 1657-1662.

The Bridges et al paper does not in fact state that “evidence for airborne transmission of seasonal influenza is lacking”, and it is our opinion that SHEA’s citation misrepresents the authors’ conclusions. Bridges et al state that evidence for airborne transmission exists, but that the relative contribution of all modes of transmission remains unclear:

“Evidence exists to support the transmission of influenza viruses by direct and indirect contact and by droplet and droplet nuclei (i.e. airborne) transmission. However, experimental studies involving humans are limited, and the relative contribution of each mode of transmission remains unclear”. (Under “Conclusions”, page 1099).

Brankston et al

There are two key problems with SHEA’s reliance on the paper by Brankston et al. The first is ambiguity relating to the meaning of “airborne transmission”, and the implications of the chosen definition for SHEA’s conclusions with respect to the necessary for use of N95 respirators for routine patient care. The second is that Brankston et al **do not** in fact conclude that “evidence for airborne transmission of seasonal influenza is lacking”.

The meaning of “airborne transmission”, and implications for N95 usage

SHEA does not define what it means by “airborne transmission”. It appears that SHEA is not referring to **close range** transmission by inhalation of droplets in or below the tracheo-bronchial size range, but rather, by “airborne transmission” SHEA means long distance transmission by small droplets:

“...pathogens which are transmitted predominantly via airborne spread by small particles that remain infective over time and may be dispersed over long distances. Such "airborne" spread is not clearly documented for influenza.”

To the extent that “airborne transmission” means “long distance transmission”, SHEA’s citation of Brankston et al is fair. However, this is a different meaning from that used by Lemieux et al and Bridges et al.

Brankston et al also state:

“We conclude that natural influenza transmission in human beings occurs over short distances rather than over long distances. In turn, because it is well documented that airborne pathogens result in infection over long distances (in

addition to close range), we conclude that natural influenza transmission occurs primarily via the droplet and contact routes". (Under "Conclusion", page 264)

When stating their belief that transmission occurs primarily via the "droplet" and contact routes, it is important to note that Brankston defines "large droplets" as those equal to or larger than "5 microns" (page 257). In other words, included within Brankston's definition of "large droplet" are the "small droplets" that are not captured by surgical masks, but instead require usage of N95 respirators.

Finally, it is worth noting that the second sentence in the above excerpt is simply a tautological statement.

Therefore, in citing Brankston, SHEA appears to be arguing that: (a) there is low risk of a health care worker contracting influenza at a "long distance" from the point of emission of influenza virus in aerosol form; and (b) close proximity transmission is caused by exposure to "large droplets" equal to or greater than 5 microns.

Argument (a) does not constitute a logical basis for concluding that N95 respirators are unwarranted for routine patient care activities that bring HCWs in close proximity to influenza patients, since in the latter scenario there is potential for exposure to aerosols that are only effectively blocked by N95 respirators.

Argument (b) is in fact an argument for use of N95 respirators, since surgical masks show significant variations in filtration efficiency in this size range.

"Evidence for airborne transmission is lacking..."

Brankston et al paper do not assert that evidence for airborne transmission is lacking. On this issue, the authors state as follows:

"Although none of the reviewed studies could specifically rule out airborne transmission, we believe that the airborne route is neither the predominant mode of transmission, nor a frequent enough occurrence to be of significant concern when considering control measures for most clinical settings".

Again, by "airborne route", Brankston et al are referring to "long distance" transmission.

7.4 N95 Respirators Provide no Higher Level of Protection over Surgical Masks

SHEA cites no authority for this assertion, and the assertion is factually incorrect. The level of particle filtration efficiency required for NIOSH certified N95 respirators is well defined, and there are valid and reliable test programs to ensure performance at prescribed levels. There are no standards for filtration efficiency for “surgical masks”, and researchers have found wide variations in their filtration efficiencies for particles in varying size ranges.

There is a considerable body of published information available on the relative efficiency of NIOSH-certified N95 masks versus “surgical masks”. The significant superiority of N95s is well established. A comprehensive review of the literature is beyond the scope of this paper, but a good synopsis is provided by the presentations given by Ann and Brosseau at the Institute of Medicine workshop on August 13, 2009.⁴⁰

7.5 Routine Use of N95 Respirators for H1N1 Patient Care Could Deplete Supplies

It is certainly a possibility that extensive use of N95s would deplete supplies, but it is not clear that this consideration alone justifies a recommendation not to use N95 respirators. If indeed the risk of HCWs contracting influenza in the absence of N95s was considered negligible, then this fact alone should be stated as justification for non-use of N95s without appeal to a marketplace shortage scenario.

However, if there is incremental occupational risk beyond the level of community acquired risk (which we consider likely to be the case), then N95 respirators should be available for use, to the extent that supplies permit. If there are concerns regarding the impact of N95 use for influenza patient care on marketplace availability, a practical response would be for organizations to stockpile and set-aside a quantity of disposable or re-usable N95s for dedicated use by HCWs providing care to patients with tuberculosis and other diseases where close proximity and long range airborne transmission is believed to occur.

7.6 Other Comments on the SHEA Position Paper

- Page 3, paragraph 1: No authority is cited for classification of various procedures as being “aerosol generating” or not. In Section 6 above we discuss the evidence relating to aerosol generation in performance of AGMPs.

⁴⁰ Roland Berry Ann. “Panel 5: Personal Protective Equipment Research on the Efficacy of Respirators in Preventing the Transmission of Influenza.” Lisa D. Brosseau. “Surgical Mask Performance.” Both presented at the Institute of Medicine Committee on Respiratory Protection Recommendations for Health Care Workers. August 11-13, 2009.

- Page 3, paragraph 3: “Transmission of influenza in acute care hospitals is a risk many magnitudes lower than the risk of community transmission and strategies that place excessive focus on preventing influenza transmission within healthcare facilities are of limited utility in an outbreak and divert attention from important community control strategies”. No authority is cited for this assertion, nor is any explanation provided.
- SHEA appears to consider H1N1 influenza to be substantially the same as seasonal influenza, in terms of mode of transmission, health impact, and risk. This is inconsistent with a recent pronouncement by the World Health Organization:

Not the same as seasonal influenza

Current evidence points to some important differences between patterns of illness reported during the pandemic and those seen during seasonal epidemics of influenza.

The age groups affected by the pandemic are generally younger. This is true for those most frequently infected, and especially so for those experiencing severe or fatal illness.

To date, most severe cases and deaths have occurred in adults under the age of 50 years, with deaths in the elderly comparatively rare. This age distribution is in stark contrast with seasonal influenza, where around 90% of severe and fatal cases occur in people 65 years of age or older.

Severe respiratory failure

Perhaps most significantly, clinicians from around the world are reporting a very severe form of disease, also in young and otherwise healthy people, which is rarely seen during seasonal influenza infections. In these patients, the virus directly infects the lung, causing severe respiratory failure. Saving these lives depends on highly specialized and demanding care in intensive care units, usually with long and costly stays.

During the winter season in the southern hemisphere, several countries have viewed the need for intensive care as the greatest burden on health services. Some cities in these countries report that nearly 15 percent of hospitalized cases have required intensive care.

Preparedness measures need to anticipate this increased demand on intensive care units, which could be overwhelmed by a sudden surge in the number of severe cases.

Source: WHO Web Site, September 8, 2009:

http://www.who.int/csr/disease/swineflu/notes/h1n1_second_wave_20090828/en/index.html

This concludes our paper.

Respectfully submitted

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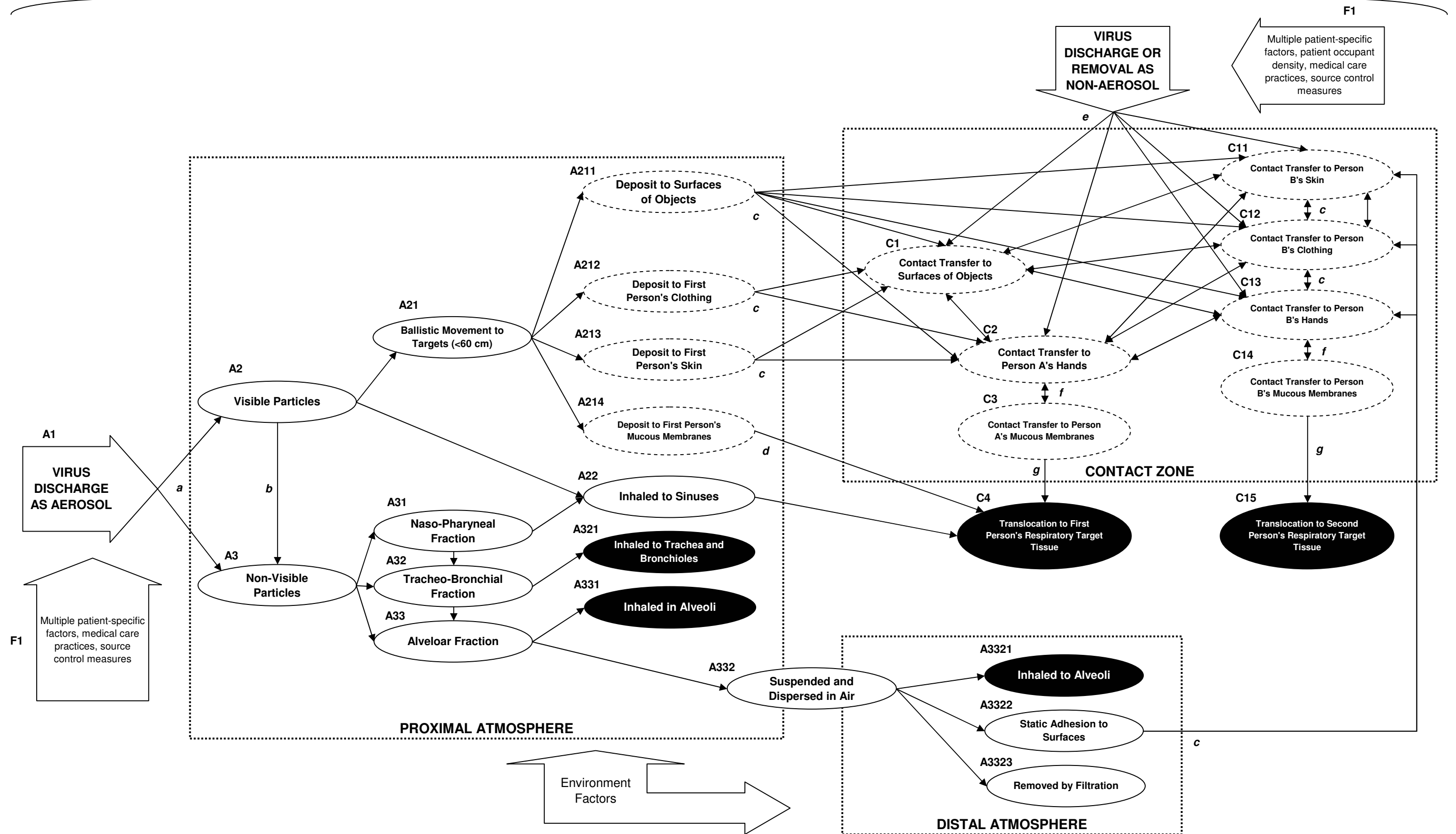
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Appendix – REA Conceptual Model of Influenza Transmission

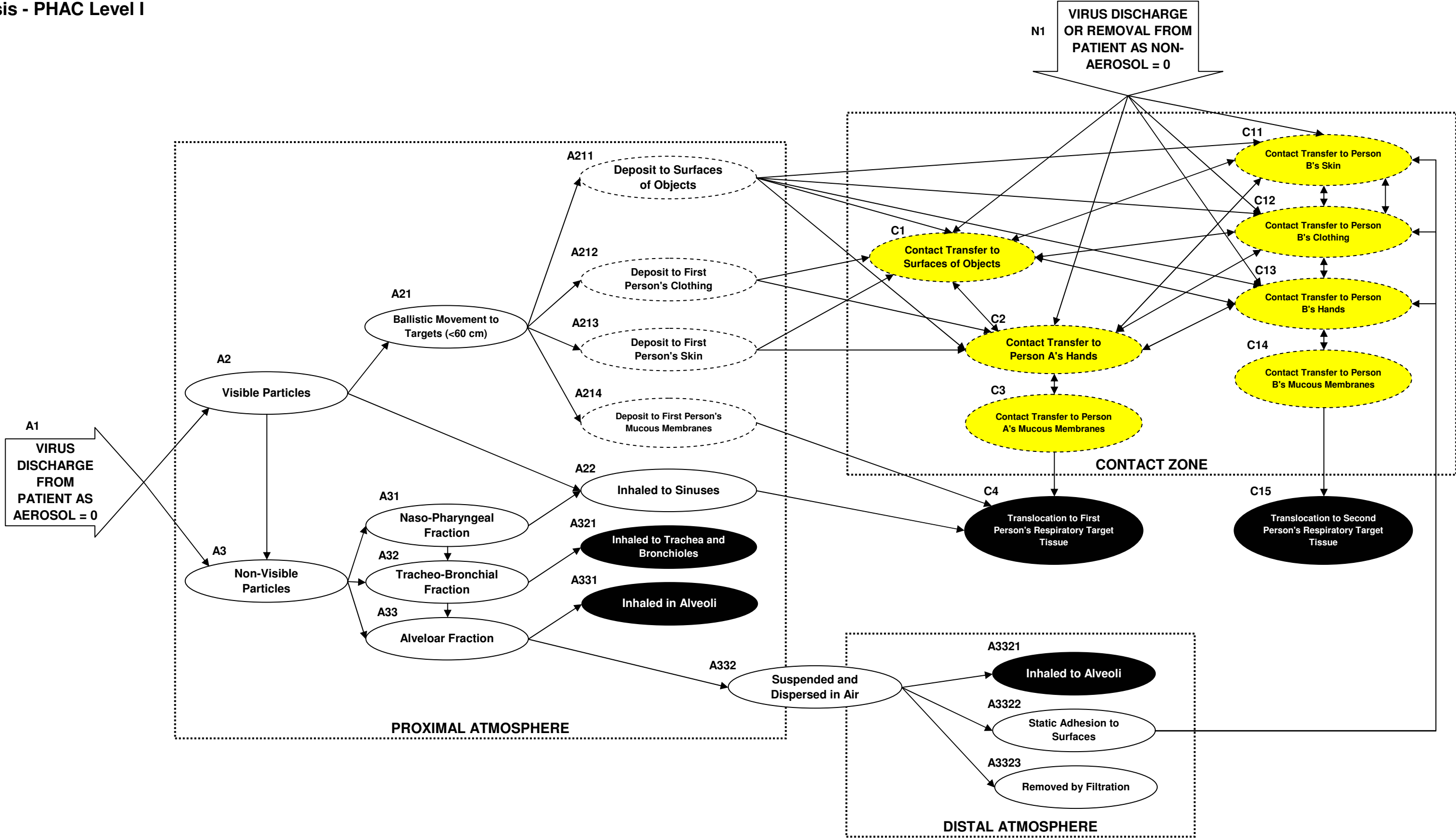
REA Model of Respiratory Virus Discharge, Dispersal and Exposure

T1 Total discharge is positively correlated to the number of dischargers, and their respective frequencies and quantities of discharge



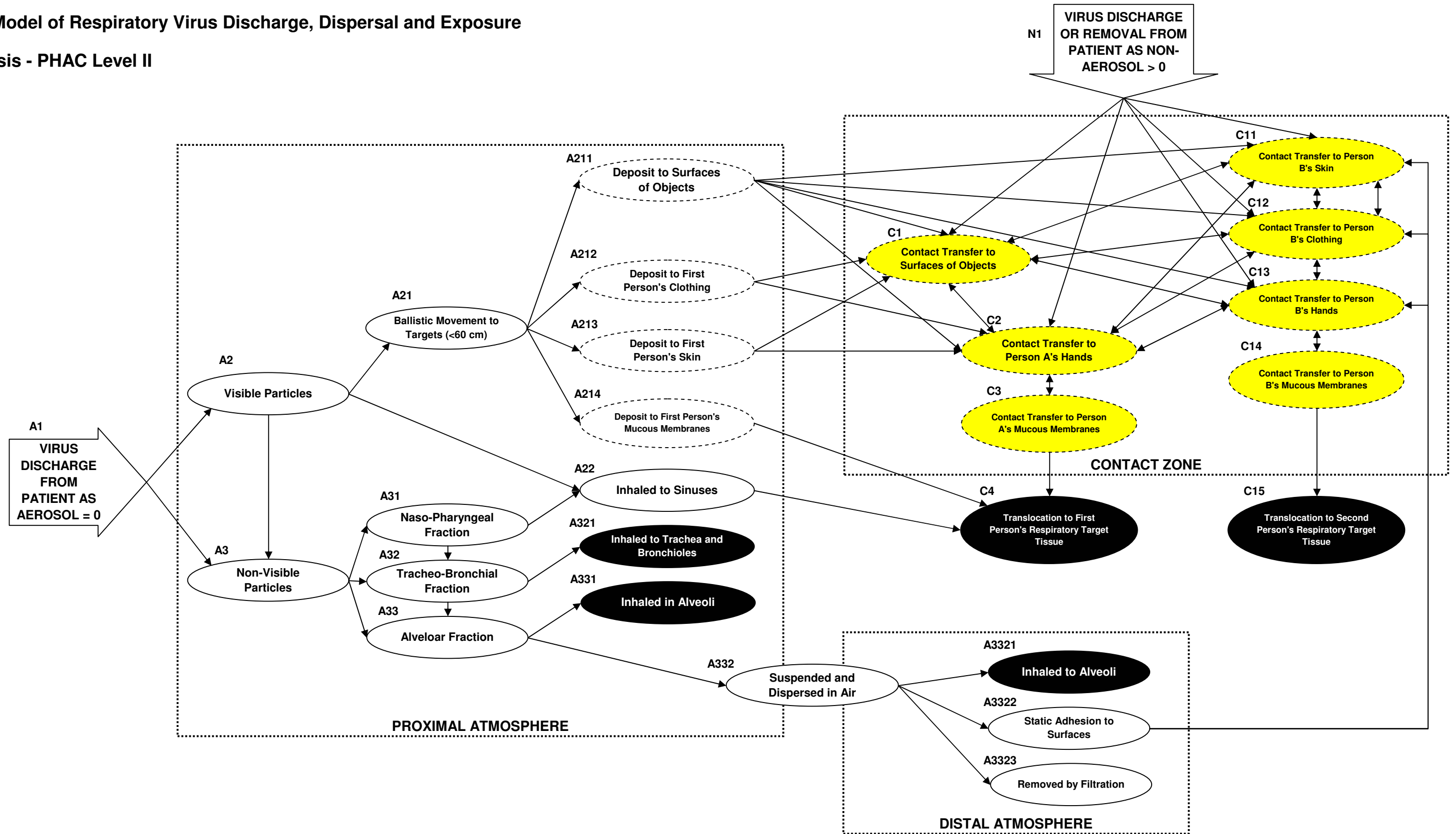
REA Model of Respiratory Virus Discharge, Dispersal and Exposure

Analysis - PHAC Level I



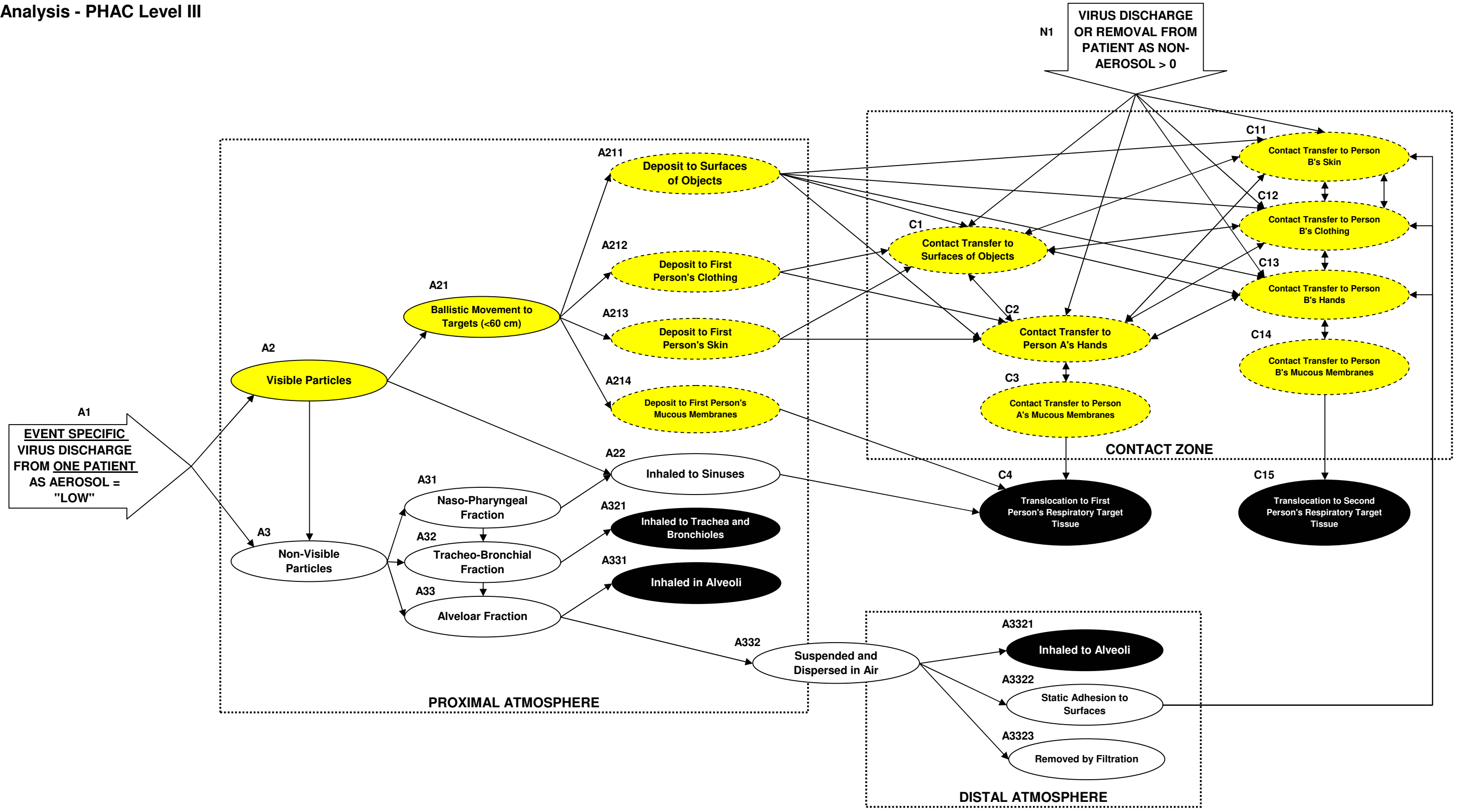
REA Model of Respiratory Virus Discharge, Dispersal and Exposure

Analysis - PHAC Level II



REA Model of Respiratory Virus Discharge, Dispersal and Exposure

Analysis - PHAC Level III



REA Model of Respiratory Virus Discharge, Dispersal and Exposure

Analysis - PHAC Level IV

