WHITE PAPER

# The Physiology of INERGEN® Fire Extinguishing Agent

INERGEN Clean Agent
Fire Suppression System

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## Introduction

INERGEN® is a gaseous fire extinguishing agent comprised of 52% nitrogen, 40% argon and 8% carbon dioxide, all of which are gases normally found in the Earth's atmosphere. It is used as a total flooding agent which extinguishes fires by diluting the oxygen concentration within an area to a point below the level that will support combustion.

The component gases of the INERGEN mixture are non-toxic. The carbon dioxide content of the atmosphere created by INERGEN agent has a well-documented, beneficial, physiological effect which stimulates respiration and enhances the efficiency of oxygen transfer from the atmosphere to the blood stream and to the brain [1,2,3,4]. Nitrogen and argon are physiologically inert at normal atmospheric pressures. The sustained breathability of the extinguishing atmosphere created by INERGEN agent is directly related to the degree of hypoxia (decreased oxygen) and hypercapnia (increased carbon dioxide).

As with all total flooding fire extinguishing agents, it is recommended that personnel evacuate the space as soon as a fire is detected. Rapid response detectors, warning alarms, sirens, and horns are used to prompt rapid evacuation, and a short time delay prior to system release provides sufficient evacuation time. With these standard precautions, exposure to the hypoxic atmosphere created by INERGEN agent will not normally occur. However, consideration must be given to situations in which an individual cannot or chooses not to evacuate.

A distinction should be made between the physiologic effects of INERGEN agent use and the effects of fire, heat, or toxins in smoke produced by combustion. The duration of safe tolerance to the toxic products of combustion will be much less than the physiologic tolerance to the non-toxic component gases of INERGEN agent [4]. In the event of unavoidable delay in evacuation, the physiologic tolerance to INERGEN extinguishing atmospheres greatly enhances the prospects of human survival without residual effect.

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With this background, it is appropriate to examine the following:

- The physiologic effect of the INERGEN extinguishing atmosphere on "normal" individuals.
- The physiologic effect of the INERGEN extinguishing atmosphere on individuals with cardiovascular or pulmonary impairments.
- The No Observable Adverse Effects Level and the Lowest Observable Adverse Effects Level for INERGEN agent.
- The physiologic effect of simultaneous exposure to INERGEN agent and to the carbon monoxide produced by the fire.

## The INERGEN Extinguishing Atmosphere

The concentration of oxygen necessary to support combustion is dependent on the fuel. Data is available on a wide range of Class B fuels. With the exception of those fuels which provide their own oxygen, extinguishment typically occurs below 14-15% oxygen [5]. This has been the basis for the successful use of carbon dioxide systems for many years.

ANSUL® has conducted a wide range of both Class A and Class B fire tests to confirm extinguishment in this range. In addition, a cup burner value for Class B fires of 29.1% has been determined for INERGEN agent on heptane, which equates to an oxygen level of 14.7%. Allowing for the required 20% safety factor, this equates to an INERGEN design concentration of 34.9%, or an oxygen level of 13.7%. The typical INERGEN design extinguishing atmosphere will be 12.0–14.0% oxygen and 3.0–4.0% carbon dioxide.

## Physiologic Effect on "Normal" Individuals

A significant body of scientific and medical data exists concerning the concurrent exposure to lowered inspired levels of oxygen and increased inspired levels of carbon dioxide. All of the referenced data is based on direct measurements in human subjects. The period of relevant research and analysis covers the 50 years from 1943-1993 [4].

Small degrees of hypoxia (low oxygen) and hypercapnia (high carbon dioxide) can be tolerated for several days without detectable adverse effect [6]. Extremely low levels of oxygen or extremely high levels of carbon dioxide can be tolerated for less than a minute [8,9,13]. Between these extremes are degrees of combined hypoxia and hypercapnia which are advantageous to the safety of occupants for durations necessary in fire protection applications [1,2,3,6,10,11,12,13,14].

Carbon dioxide in the concentrations present in the INERGEN extinguishing atmosphere promptly improves tolerance to even severe degrees of hypoxia [1,2,3]. This is the result of the combined effects of three normal physiologic control mechanisms. They are: (a) stimulation of respiration, which increases arterial blood oxygen content and partial pressure, (b) dilation of brain blood vessels, which increases brain blood and oxygen flow, (c) a shift in the hemoglobin dissociation curve, which aids unloading of oxygen in all tissues [1,14,16].

Over the range of oxygen reduction to be encountered in fire extinguishment, the tolerance of normal individuals to hypoxia is improved by simultaneous exposure to increased carbon dioxide levels [1,2,3,14,17,18]. Carbon dioxide increases brain blood flow and oxygenation at all levels of inspired oxygen [2,14,19,20]. The beneficial effects of added carbon dioxide over the range created with INERGEN agent may be accompanied by some respiratory discomfort, but will not prevent purposeful mental or physical activity, and is readily reversible without residual effect [4,14].

Because of the constant ratio of carbon dioxide to inert gases in INERGEN agent, there is an automatic adjustment toward increased levels of carbon dioxide as oxygen levels are reduced through the application of increasing amounts of INERGEN agent. This is clearly physiologically appropriate.

The applicable scientific literature and medical data is vast. Several examples are given to provide a sampling of the available data. Complete reference documentation is available upon request.

- Twenty minute exposures to air at 5400 meters (17,717 ft) altitude (equivalent to 10.5% oxygen), with 3.5% carbon dioxide, rapidly relieved severe symptoms of acute altitude sickness [18].
- Prolonged (50-60 hour) exposure of 77 people to increasing carbon dioxide with decreasing oxygen was tolerated at rest and at moderate exercise without significant performance decrement. Highest inspired carbon dioxide was 6.7%, lowest oxygen concentration was 10.45%. Duration at oxygen level of 12.2% and over 5% carbon dioxide was 40 hours [6].

## Physiologic Effects On Individuals With Impairments

Specific experiments have not been conducted concerning the tolerance of individuals having heart or lung abnormalties to INERGEN agent or any other extinguishing agent, nor are they likely to be performed. It was therefore necessary to obtain practical clinical judgment concerning situations of risk for such impaired individuals in the workplace. Such an evaluation has been conducted by clinical and research specialists at the University of Pennsylvania Medical Center [21], and has been peer reviewed for the U.S. Environmental Protection Agency (EPA) by specialists at:

- University of Rochester Medical Center (Pulmonary and Critical Care Unit)
- National Institute of Health (Department of Neurological Disorders and Strokes)
- Temple University Medical Center (Cardiology Section)

All of the reviews were favorable. This, together with physiological research information obtained in normal individuals [14], has led the U.S. EPA to approve INERGEN agent for normally occupied spaces.

For individuals with abnormalities of heart, circulation or lung, only their prompt exit from the space involved in fire and extinguishment is considered rational. If assistance is not normally required, it is unlikely to be needed as a specific consequence of INERGEN flooding [21]. The time course for changes of oxygen and carbon dioxide levels within the human organism (body) are in the order of several minutes. The full degree and effect of long duration exposure to hypoxia will not occur within the first several minutes after the first breath of a low oxygen atmosphere. Therefore, physiologic changes will not interfere with exit procedures, even for individuals with circulatory or pulmonary impairment [21].

Specific clinical abnormalities researched include:

- Coronary vascular disease.
- Cardiac decompensation.
- Cardiac arrhythmia.
- Cerebral vascular accident (stroke).
- Pulmonary emphysema.

For the above conditions, review by medical scientists of the Environmental Biomedical Research Data Center at the University of Pennsylvania concludes that persons handicapped by degrees of cardiac or pulmonary abnormality not limiting capability for normal entry and exit at work will be able to exit during INERGEN flooding, with any transient exposure completely reversing itself upon exposure to the external atmosphere [21].

## No Observable Adverse Effects Levels and Lowest Observable Adverse Effects Levels

The No Observable Adverse Effects Level (NOAEL) and Lowest Observable Adverse Effects Level (LOAEL) are defined for halogenated agents based on cardiac sensitization, which is generally accepted to be the first adverse toxicological effect to be observed [22]. Cardiac sensitization is not an appropriate basis for establishing a NOAEL for inert gases. Indeed, the concept of a NOAEL may not be appropriate in this instance. However, to allow conformance to and consistency with the NFPA 2001 document, data has been provided to establish both a definition of NOAEL for inert gases and a NOAEL value for INERGEN agent.

For inert atmospheric gases, which are not inherently toxic, the first adverse effect observed as a result of the hypoxic atmosphere created will be a reduced oxygen supply to the brain, compensated in part by the improvement in brain blood flow produced by the carbon dioxide component. If sufficient in degree the reduced oxygen supply will manifest as a decrease in aspects of brain functions such as judgement, decision-making, and brain metabolism [1,13,16,17,20,23]. Although these decremental effects are not as serious as cardiac sensitization, they do provide the basis for establishing a NOAEL.

The time basis for cardiac sensitization evaluation is exposure of test animals (dogs) for a period of 5 minutes. It is recommended that the time basis for exposure to the hypoxic atmosphere created by inert gases also be set at 5 minutes, although medical studies indicate that human subjects can tolerate exposure periods of 15 minutes or more. A recommended definition of the NOAEL for inert gases is: **The highest concentration of agent for which no adverse physiologic effect has been observed due to inhalation of the resulting hypoxic atmosphere.** The specific adverse physiologic effect would be an observable decrease in brain function exhibited as a decrement in judgement and decision capability sufficient to negatively impact the ability to react properly in a fire situation.

For INERGEN agent, the NOAEL is 52% creating an atmosphere with 10% oxygen and a corresponding carbon dioxide concentration of 4.5–5.5%. Medical studies have indicated that when breathing an atmosphere containing 10% oxygen and 5.5% carbon dioxide, the oxygen partial pressure, oxygen content, and hemoglobin oxygen saturation of brain venous blood is equivalent to levels existing with normal air breathing [1,3,13,14]. Subjects exposed to oxygen levels of 10% and less, with and without 5% carbon dioxide, showed normal intellectual function at 10% oxygen and 5% carbon dioxide, but exhibited confusion and loss of mental responses without the added carbon dioxide [1].

The time course of equilibration of oxygen levels in the brain blood flow is in the order of several minutes. Thus, a five-minute exposure to the NOAEL hypoxia level of 10% oxygen would only occur after the warning and time delay period and after discharge of a sufficient quantity of inert gas agent to lower the oxygen to this level, and even then would be further buffered by the time required for physiologic equilibration.

The corresponding definition for LOAEL is: **The lowest concentration of agent for which an adverse physiologic effect has been observed due to inhalation of the resulting hypoxic atmosphere.** Again, the time course for exposure is 5 minutes.

For INERGEN agent, the LOAEL is 62% corresponding to an atmospheric oxygen level of 8% and a carbon dioxide level of 5.0–6.0%. This is an increased degree of hypoxia relative to the 10% oxygen atmosphere existing at the INERGEN NOAEL level. Studies have indicated that even lower levels of oxygen are tolerable in the presence of carbon dioxide [1,3,16,18]. An accompanying sensation of breathlessness could limit the maximum degree of physical exertion, but will not cause failure of physical exit or escape capability [4]. During exposures to 6.5-8.5% oxygen in the presence of appropriate added inspired carbon dioxide, mental function and consciousness remained for longer than the planned 30 minutes of the study [9].

Lending further support to both the NOAEL and LOAEL levels are medical studies measuring the percent of brain venous hemoglobin oxygen saturation (HOS) as an index of overall brain oxygenation. For a group of subjects whose average brain venous HOS was 60.2% when breathing 20% oxygen, the brain venous HOS actually rose slightly to 62.1% when breathing an atmosphere of 10% oxygen and 5% carbon dioxide. When the atmosphere was changed to 8% oxygen and 5% carbon dioxide, the brain venous HOS decreased to 57.1%. For comparison, the brain venous HOS at 10% oxygen without carbon dioxide was 44.8%, and at 8% oxygen it was 39.4% [1].

Oxygen levels below 8% have been studied, both with and without added carbon dioxide. In all cases the added carbon dioxide is advantageous [1,4]. The results of specific research in non-exercising individuals has shown that breathing 5% carbon dioxide during acute exposure to 6, 5 or 4% oxygen in nitrogen maintains consciousness and normal electroencephalogram [1,3].

In all cases, the medical data has been collected on human subjects exposed for periods far in excess of the exposure times for fire protection purposes.

## Physiologic Effects of Exposure to Carbon Monoxide in the Presence of INERGEN Agent

The concurrent events of fire, production of carbon monoxide (CO), and use of INERGEN agent to prevent both, can expose occupants simultaneously to the lowering of atmospheric oxygen with increase in carbon dioxide, and to small or significant concentrations of carbon monoxide. Limitations of duration of exposure are less critical for INERGEN components than for hazards of fire or CO. Again it should be stressed that evacuation is recommended and should occur in all fire situations. **Accidental discharge events not accompanied by fire will, of course, not involve carbon monoxide (CO) exposure.**

Factors affecting the rate of uptake of carbon monoxide into the blood from the atmosphere to replace oxygen and form CO hemoglobin have been firmly established since the mid-1940's [8,15,24,25]. They include inspired CO concentration, duration of exposure to it, and respiratory volume per minute. The high affinity of CO for hemoglobin allows competition with oxygen for combination with hemoglobin [8,24,26]. In the initial stage of a fire situation, including early post alarm, CO levels will be low, but will rise later.

The effect on rate of CO uptake due to increased respiratory ventilation produced by the factors of hypoxia, carbon dioxide, and activity is relevant to INERGEN agent use [11,27]. Adding carbon dioxide to 14, 12, or 10% respired oxygen produces the desired positive increase in respiratory ventilation [28]. The balance between desired improvement in physiologic tolerance to hypoxia and undesired influence on CO uptake is favorable during the early period of useful exposure, since CO uptake is time dependent.

The nature of symptoms of increased CO hemoglobin depends upon degree and duration. The hypoxic effect of CO uptake and CO hemoglobin formation does not lower arterial oxygen partial pressure, stimulate respiration, nor produce symptoms of respiratory distress. The normal actions of carbon dioxide inhalation will decrease the hypoxic symptomatic effects of carbon monoxide by increasing arterial oxygen partial pressure and brain blood (oxygen) flow, and by providing an aid to the release of oxygen in the tissues [26].

Testing conducted both in Europe and in the United States has shown that fires of significant size relative to room volume and subsequently extinguished by INERGEN agent will generate carbon monoxide levels of approximately 400-600 ppm. Assuming an inhalation (ventilation) rate of 40 L/minute, this would create a CO hemoglobin level of approximately 14% after a 15 minute exposure [4].

Human subjects have been studied at sea level under conditions of vigorous exercise with induced CO hemoglobin levels of 20 to 30% without comment concerning symptoms [3,10].

Symptoms in 78 CO exposures of 20 to 66 minutes in air at sea level produced no subjective symptoms until CO hemoglobin exceeded 15%. From 15% to 25%, symptoms comprised mild-to-moderate headache, "giddiness," and on a few occasions, slight nausea [25]. In relation to practical situations with composite effects of atmospheric hypoxia and carbon monoxide exposure, 15% CO hemoglobin has been considered a clearly tolerable level not producing serious symptoms, even when in the presence of INERGEN hypoxia design concentrations [4,11,27]. In such practical situations each of the effects of atmospheric carbon dioxide that improve brain oxygenation serves to counter the hypoxia induced by carbon monoxide alone.

In none of the medical research examples cited would exit procedures be handicapped for typical individuals. Upon exit, CO hemoglobin levels, hypoxic effect and symptoms diminish [4].

## Summary

Since INERGEN agent is nontoxic in and of itself, the physiologic concerns to be evaluated are those related to inhalation of the atmosphere that INERGEN creates. The extensive medical studies conducted to evaluate breathing atmospheres for mountain climbing, deep sea diving, and high altitude flight provide a wealth of data directly applicable to INERGEN atmospheres. The references cited in this summary indicate that:

- Typical individuals will not be adversely affected by exposure to INERGEN agent, even for prolonged periods of time.
- Individuals with pre-existing cardiac or pulmonary impairments will not be adversely affected by INERGEN agent during the time needed for exit, nor will INERGEN agent reduce their ability to exit.
- The recommended NOAEL and LOAEL for INERGEN agent are 52% and 62% respectively, equivalent to oxygen levels of 10% and 8%, and corresponding levels of carbon dioxide.
- Because carbon monoxide reduces the oxygen available to the brain by combining with hemoglobin, the increased blood flow and oxygen delivery to the brain that is created by the carbon dioxide in INERGEN agent will act to counter the effects of carbon monoxide.

*Typical individuals will not be adversely affected by exposure to INERGEN agent, even for prolonged periods of time.*

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