

Infrasound

Brief Review of Toxicological Literature

November 2001

Preface

(Revised March 2002)

Recent interest in the potential adverse human health effects of infrasound (generally inaudible sound with a frequency of <20 Hz) arises from health concerns expressed by the residents of Kokomo, Indiana. Several individuals in this community have complained of subjective non-specific symptoms including annoyance, sleep disturbance, headaches, and nausea. These symptoms are perceived by the individuals to be due to a low-frequency hum-like noise in and around their homes that is not clearly audible to everyone. Several local, state, and federal agency officials as well as acoustic experts in the academic community and private sector have been called upon to assist in investigating these health complaints. As yet, no firm conclusions have been reached regarding the relationship between this low-frequency noise and the residents' health complaints.

Subsequent to inquiries from the U.S. Senators from Indiana, the National Institute of Environmental Health Sciences (NIEHS) agreed to review the existing scientific literature on the health effects of infrasound. This review was intended to serve as an initial step in determining whether sufficient information is available to make a reasonable assessment of the potential for adverse human health effects to occur as a result of infrasound exposure. Consequently, the NIEHS is nominating toxicological studies of infrasound for consideration by the National Toxicology Program (NTP) to seek broad federal agency and public input regarding the need for further federal sponsored experimental animal toxicology research on this environmental agent.

This document briefly summarizes studies identified in the open literature relating to the biological and other effects of infrasound exposure in humans and laboratory animals. The literature searches were performed in August-September, 2001 and the search strategy is briefly described in *Section 5.0*. Over one hundred relevant studies were identified that differed widely in their experimental design and selection of endpoints for evaluation. This study variability somewhat limits the conclusions that can be drawn regarding the potential to cause adverse health effects in humans without further expert evaluation and review.

The measurement of intensity of sound is the sound pressure level (SPL), usually given in decibels (dB). Sound is a complex physical phenomenon and no attempt is made here to describe in detail acoustic principles or methods for the measurement of sound. Furthermore, the physiological and psychological effects of higher frequency sound and noise comprise an enormous volume of literature and have not been reviewed at this time. This literature is relevant because effects of different sound frequencies could be similar and because in environmental settings human exposure to infrasound rarely if ever occurs in the absence of exposure to other sound frequencies.

Many of the infrasound studies identified in the literature search are not available in English or are otherwise difficult to acquire, and thus not all articles have been obtained at this time. The individual study summaries are presented as an annotated bibliography and in many cases are based only on review of an English abstract. Attention has not been given to an evaluation of individual study quality or to the strength of the overall evidence regarding potential adverse health effects. This would require a more thorough and independent expert review to draw conclusions regarding adverse human health effects attributable to infrasound exposure. Rather, the document focuses on identifying and describing the available literature regarding reported physiological and/or psychological effects of infrasound. This document has not been formally peer-reviewed at this time.

Experimental studies have been reported where humans or various species of animals (rats, mice, guinea pigs, chinchillas) have been exposed to infrasound in the laboratory. Most of the studies identified involved exposures at 90 dB and higher and ranged from minutes to several months. Of the many animal studies identified, there were none involving long-term (six months or greater) exposure and few that employed modern toxicology testing protocols and pathological assessments. The most common endpoints studied were behavioral, sensory, or simple physiological (e.g. blood pressure) changes. Some studies focusing on biochemical, cellular, or morphological changes in organs and tissues were identified. There were few studies evaluating reproductive function, developmental effects, and immunological effects, and no studies that evaluated carcinogenic effects.

Most studies reported some effects attributed to infrasound exposure, though many studies also reported no observable effects. Among the more consistent findings in humans were changes in blood pressure, respiratory rate, and balance. These effects occurred after exposures to infrasound at levels generally above 110 dB. Physical damage to the ear or some loss of hearing has been found in humans and/or animals at levels above 140 dB. As many studies evaluated endpoints that may or not necessarily be considered adverse, a careful evaluation of the biological significance and reversibility of any reported findings is critical. Due to differences in auditory

perception and physiological response to sound, the relevance of animal studies to assessing potential human effects must also be carefully evaluated. An evaluation of consistency in reported effects among the different studies identified is made difficult due to limited details available for this review on methods of generating infrasound, characterization of the experimental exposures, and methods of assessing biological effects. For example, other sound frequencies may have been present in some experiments and effects of exposure to pure tones versus broadband frequency may be different. Thus, it is not clear if "environmental" infrasound, in terms of intensity level, frequency range, and frequency composition, has been adequately reproduced in laboratory experiments.

In summary, though a number of biological effects have been reported that are attributed to infrasound exposure in experimental settings, any assessment of potential adverse human health effects resulting from environmental infrasound exposure is hampered by numerous gaps in our current knowledge. Examples of critical data gaps include a lack of high quality long-term experimental studies of infrasound, and inadequate characterization of environmental infrasound and accompanying higher frequency sound levels in community settings. Thus, this document may serve as a starting point for determining what types of experimental toxicology research or testing may be useful for further characterizing potential adverse health effects of infrasound exposure in humans.

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Executive Summary

Infrasound is acoustic energy with frequencies up to 20 Hertz (Hz), having wavelengths of 17 m or more. Some definitions give the upper limit of 16 Hz; others restrict infrasound to delivery by air transmission. Infrasound is seldom generated at high sound pressure levels (SPL; usually measured in decibels [dB]) without accompanying audible sound (1). However, hearing protection, e.g. ear muffs and ear plugs, offers little protection against infrasound exposure (2,3).

Infrasound exposure is ubiquitous in modern life. Infrasound is generated by natural sources such as earthquakes (4) and wind; means of transportation such as automobiles, trucks, aircraft, watercraft, and rail traffic (4-6); certain therapeutic devices (which do not meet the restriction of infrasound to airborne delivery) (7-16); numerous industrial sources such as heavy machinery and air compressors; air heating and cooling equipment; and household appliances such as washing machines (1,5,6,17). The potential use in nonlethal acoustic weapons is discussed briefly (18-20).

OSHA guidelines for occupational noise exposure are concerned with SPL limits (90 to 115 dB(A) for 8 hours to 0.25 hour), not frequencies (21). The American Conference of Governmental Industrial Hygienists (ACGIH) recommends that except for impulsive sound with durations of less than 2 seconds, one-third octave levels for frequencies between 1 and 80 Hz should not exceed a SPL ceiling limit of 145 dB, and the overall unweighted SPL should not exceed a SPL ceiling limit of 150 dB; no time limits are specified for these recommended levels (22). NASA criteria for noise exposure in space craft and space stations include a limit of 120 dB for 24-hour exposure to 1 to 16 Hz (23).

Literature retrievals from several biomedical databases, the National Technical Information Service (NTIS) file, and the Internet required the inclusion of the words infrasound or infrasonic. The presentation of the information in the toxicology section is in the style of an annotated bibliography. The human studies subsection is not comprehensive and includes only selected studies identified in the open literature. All of the 59 animal toxicity studies identified in the literature searches are included, but the subsection is not totally comprehensive. A few additional publications were cited in some of the references. A large fraction of the annotations are based on the authors' abstracts in the database records. Annotations for many of the Russian studies were based on limited data extraction from the original [non-English] articles since the database records frequently did not have abstracts.

Summary of Studies in Humans

The literature search identified 69 studies, 34 of which are in English. The records for about half of the foreign-language publications do not have abstracts. Altogether, only two-thirds of the records have abstracts. Twenty-four of the identified human studies are included in the annotated bibliography. Of these, references for 6 citations have been retrieved. English abstracts are available for 15 citations. The effects studied were on the cardiovascular (the myocardium) and nervous systems, eye structure, hearing and vestibular function, and endocrine modulation. Specific CNS effects studied included annoyance, sleep and wakefulness, perception, evoked potentials, electroencephalographic changes, and cognition.

The primary effect of infrasound in humans appears to be annoyance (24-26). To achieve a given amount of annoyance, low frequencies were found to require greater sound pressure than with higher frequencies; small changes in sound pressure could then possibly cause significantly large changes in annoyance in the infrasonic region (24). Beginning at 127 to 133 dB, pressure sensation is experienced in the middle ear (26). Regarding potential hearing damage, Johnson (27) concluded that short periods of continuous exposures to infrasound below 150 dB are safe and that continuous exposures up to 24 hours are safe if the levels are below 118 dB.

There is no agreement about the biological activity of infrasound. Reported effects include those on the inner ear, vertigo, imbalance, etc.; intolerable sensations, incapacitation, disorientation, nausea, vomiting, and bowel spasm; and resonances in inner organs, such as the heart.

Infrasound has been observed to affect the pattern of sleep minutely. Exposures to 6 and 16 Hz at levels 10 dB above the auditory threshold have been associated with a reduction in wakefulness (28). Workers exposed to simulated industrial infrasound of 5 and 10 Hz and levels of 100 and 135 dB for 15 minutes reported feelings of fatigue, apathy, and depression, pressure in the ears, loss of concentration, drowsiness, and vibration of internal organs. In addition, effects were found in the central nervous, cardiovascular, and respiratory systems (29). In contrast, a study of drivers of long distance transport trucks exposed to infrasound at about 115 dBA found no

statistically significant incidence of such symptoms (e.g., fatigue, subdued sensation, abdominal symptoms, and hypertension) (30).

Studies have shown that infrasound (6 to 16 Hz at levels ranging from 95 to 130 dB and up to an exposure time of one hour) causes an increase in diastolic blood pressure and decreases in systolic blood pressure and pulse rate (31). Long-term exposure of active Swiss airforce pilots to infrasound with a frequency of 14 or 16 Hz at 125 dB produced the same changes. Additional findings in the pilots were decreased alertness, faster decrease in the electrical resistance of the skin compared to unexposed individuals, and alteration of hearing threshold and time perception (32). However, a whole-body exposure to infrasound at 10 and 15 Hz (level not provided) did not produce changes in respiration, pulse, and blood pressure (33).

In several experiments to assess cognitive performance during exposure to infrasound (7-Hz tones at 125, 132, and 142 dB plus ambient noise or a low-frequency background noise for up to 30 minutes), no reduction in performance was observed in the subjects (34). Sole exposure to infrasound at 10 to 15 Hz and 130 to 135 dB for 30 minutes also did not produce changes in autonomic nervous functions (35). The ability of infrasound (5 and 16 Hz at 95 dB for five minutes) to alter body sway responses suggested effects on inner ear function and balance (36).

Summary of Studies in Laboratory Animals: Acute Exposure Duration

Citations for 31 acute animal studies are annotated in this section; 9 of the references have been retrieved and are available in English. English abstracts are available for an additional 5 references.

Studies of infrasound up to 124 dB for up to four hours found transient effects in behavior, brain chemistry, and effects on blood vessels. Studies at higher SPL induced cochlear damage and other morphological damage in the ear. Thus, rats exposed briefly to infrasound around 120 dB showed changes in concentrations of acetylcholine (37), acetylcholinesterase, brain glutamate (increases) (38), and brain norepinephrine and dopamine (decreases) (39,40). Gastric mucosal blood flow decreased (41) and organ tissue permeability increased (42). At about 100 dB, rats showed reduced endurance in already poor treadmill performers (43), performance decrements in acquisition and retention of conditioned reflexes, and somnolence (44). Acute exposure of mice to ethanol plus infrasound reduced time to submersion in forced swimming tests (45-47). A one-hour exposure to 20 Hz at up to 133 dB SPL did not induce the cochlear and hair cell damage observed in guinea pigs that had been exposed to 163 dB SPL. No morphological changes were observed up to 140 dB (48,49). Infrasound exposure induced endolymph displacement, altered the endonuclear potential (50,51), and reduced the amplitude of the auditory evoked potential and prolonged its latency time in guinea pigs (52). Continuous or intermittent infrasound exposure of chinchillas at 150 to 170 dB induced considerable damage in the ear, including tympanic membrane perforation, bleeding, hair cell damage, saccular wall rupture, Reissner's membrane rupture, and endolymphatic hydrops (53). Continuous exposure was responsible for most of the incidences of several of these endpoints. Too few data were included about rabbit and monkey experiments for summarization.

Summary of Studies in Laboratory Animals: Short-Term Exposure Duration

Twenty short-term studies have been annotated. Full articles in English are available for 8 of the references. Abstracts in English are available for 11 additional citations.

In the short-term animal studies with exposures up to 145 Hz for up to four months, adverse effects were noted on the morphology, histopathology, and histochemistry of the cardiovascular system, nervous system, the ears, the liver, and other organs.

Rats exposed to 8 Hz at 120 dB for up to 45 days showed myocardial cell pathology, microcirculation disturbances, ischemia, and mitochondrial destruction in capillaries (54). Rats exposed to 10 to 15 Hz at 135 to 145 dB for 45 days showed arterial constriction, nuclear deformation, and mitochondrial damage. Regeneration occurred after exposure stopped (55). Rats exposed to 8 or 16 Hz at 120 to 140 dB for up to 40 days showed reduced oxidation-reduction (redox) enzymes in the myocardium, disturbed blood flow, myofibrillar fragmentation, and RNA and DNA changes. Regeneration began within 40 days after infrasound exposure ceased (54,56). Exposure of rats to 8 Hz at 115 and 135 dB for four months induced morphological changes in the myocardial ultrastructure; significant decreases in succinate dehydrogenase and myocardial adenosine triphosphate (ATP) and adenosine diphosphate (ADP); and significant increases in α -ketoglutarate dehydrogenase, myocardial adenosine monophosphate (AMP), and plasma corticosterone (57).

Rats exposed to 8 Hz at 100 dB for up to 60 days showed biochemical and morphological changes in blood and

tissues, including dystrophic tissue changes in the lungs, liver, kidneys, heart, adrenals, and testicles. Imidazole treatment reduced the dystrophic tissue changes and changes in enzyme concentrations (58). In studies of infrasound-induced histopathological and morphological changes in the liver after 40-day exposures, the most damage was observed at 8 and 16 Hz at 140 dB. Damage included strongly deformed nuclei, lysis and vacuole formation in the cytoplasm, and lipid granules in the cytoplasm (59). Exposure of rats to 8 Hz at up to 140 dB for 25 to 45 days caused irreversible changes in hepatocytes (60). Exposures of 8 and 16 Hz at up to 140 dB for up to 35 days induced fluctuations in heart and liver enzyme levels.

Exposure of rats to 8 Hz at 110 dB for ten weeks induced transient changes in working capacity and oxygen requirements, increased unconditioned reflexes, and induced immunological effects (61). Exposures to 8 Hz at 120 and 140 dB for up to 40 days induced changes in the heart, neurons, and auditory cortex that increased in severity with length of exposure (62). Exposures to 8 Hz at 100 and 140 dB for up to 25 days affected conjunctival blood vessels. Capillaries initially constricted and an increased permeability of blood vessels led to capillary and tissue swelling (63). Exposure to 4 Hz at 110 dB for 40 days induced ear damage worse than that observed after exposure to 31.5 or 53 Hz at 110 dB for 40 days. Alkaline phosphatase activity was reduced in the blood vessels of the stria vascularis and their permeability was impaired. The infrasound exposure induced neurosensory hearing impairment (64).

Mice exposed to 8 Hz at 120 dB showed erythrocyte-filled acini and thickening of the inter-alveolar septa of the lungs. Exposures of 8 and 16 Hz at 140 dB ruptured blood vessel walls and destroyed acini (65).

Guinea pig short-term studies reported ear damage. Exposure to 4 Hz at 110 dB for 40 days increased alkaline phosphatase concentrations in vessels of tympanic membranes (66). Exposures to 8 or 16 Hz at 90 to 120 dB for up to 25 days induced morphological changes in receptor cells and hair cells of the inner ear. These changes and changes in the endoplasmic reticulum and mitochondria recovered after exposure ended (67).

Rabbits exposed to 10 Hz at 100 to 110 dB for 24 days showed disturbances of enzyme levels of the mitochondria and reduced contractile function of the myocardium (68).

Summary of Other Animal Studies

Synergistic and antagonistic effects were reported in several of the acute and short-term animal studies. Two articles and 3 abstracts are available in English. Diazepam (39), ethanol (46,47,69), imidazole compounds (58), ascorbic acid (69), and microwave radiation (61) moderated the adverse effects of infrasound exposure.

Nine citations covering reproductive and developmental effects, carcinogenicity, genotoxicity, immunotoxicity, and other studies were considered for this report. English abstracts are available for 3 of these studies.

The only finding relating to reproductive effects was dystrophic changes in rat testicles (58).

No studies were identified on subchronic and chronic toxicity, carcinogenicity, anti-carcinogenicity, and initiation/promotion of cancer. Details for a study of genotoxicity in rat bone marrow cells have not been reviewed.

Infrasound pretreatment (10 Hz, 155-160 dB) made guinea pigs less sensitive to antigen induction of anaphylactic shock (70). Infrasound exposure of rats and rabbits to 8 Hz at 115 dB enhanced the immunotoxic effects of gamma radiation on cell and humoral immunity and on autoimmune processes (71).

In an *in vitro* study, ATPase activity in rat whole blood decreased at 16 Hz at 120 dB but increased at 2 Hz. Superoxide dismutase (SOD) concentrations increased with increasing frequency (72).

1.0 Introduction

Infrasound comprises soundlike waves of acoustic energy with frequencies of 20 hertz (Hz), the audible limit, and below. Some sources give the upper limit of infrasound frequencies as 16 Hz. The definition of infrasound may be limited to airborne acoustic energy at these frequencies. The wavelengths of 17 m or more can travel for long distances. The measurement of intensity of infrasound is the sound pressure level (SPL), usually given in decibels (dB). Sound levels are computed in dB-SPL by using the average intensity. One phon is 1 dB-SPL at 1 kHz. Other units for sound pressure levels are explained at the Stanford University web site http://ccrma-www.stanford.edu/~jos/r320/DB_SPL.html (4,73). Perception of low-frequency sound in the range 2 to 100 Hz is comprised of both aural and tactile sensations. High pressure levels may induce resonance responses in body cavities (74).

2.0 Sources and Exposure

Infrasound like all sound is ubiquitous in modern life; e.g., it is generated by motor vehicles, aircraft, watercraft, trains, hydroelectric power stations, compressors, and industrial equipment (6). Intense infrasound exposure is generally accompanied by exposure to intense sounds above 20 Hz (75). In fact, infrasonic acoustic energy does not usually occur in the absence of sounds within the normal audible range due to the processes in which such sounds are generated (1). Ear plugs and ear muffs may not offer sufficient protection (3). Protective equipment usually does not stop penetration of infrasound (2). Ear muffs may even amplify infrasonic frequencies (1).

2.1 Natural Sources

Infrasound is generated by thunder, earthquakes, large waterfalls, ocean waves (< 1 Hz), wind (up to 135 dB at 100 km/h; up to 110 dB at 25 km/h), fluctuations in atmospheric pressure (< 1 Hz at 100 dB), and volcanos (4). Running generates infrasound at frequencies below 2 Hz at levels up to 90 dB; swimming also generates infrasound below 2 Hz, but the pressure is more intense (up to 140 dB).

2.2 Vehicles

Riding in automobiles exposes drivers and passengers to 1 to 20 Hz at up to 120 dB. Exposures while riding in helicopters, other aircraft, submarines, and rockets range from 1 to 20 Hz at 120 to 145 dB. In a free field, diesel engines generate frequencies of 10 to 20 Hz at sound pressure levels up to 110 dB. Jet engines, helicopters, and large rockets generate frequencies of 1 to 20 Hz at 115 to 150 dB (4). In a Finnish survey (5), infrasound levels exceeding 120 dB were found in cars and railway engines. The usual range in vehicles with closed windows was 90 to 110 dB. Infrasound sound pressure levels in aircraft cockpits and cabins ranged from 80 to 100 dB. Ships and aircraft sonic booms are other vehicular sources (1). In Japan, Okada (17) measured infrasound at 83 dB at 20 m from a running truck and 100 dB at 20 m from a running railroad carriage. Thus, persons may be subjected frequently to the annoyance of infrasound exposure if they reside in the vicinity of heavily trafficked areas, railways, airports, or rocket launch sites. Drivers, pilots, and other transportation workers are among those occupations with considerable exposure.

2.3 Therapeutic Devices

Several Russian and European publications report on therapeutic applications of infrasound. A few examples are given in this brief discussion. Infrasound pneumomassage at 4 Hz (daily 10-minute sessions for 10 days) stabilized the progression of myopia in school children (13). Infrasound phonophoresis (frequency and sound pressure level not provided) of antibacterial drugs in the treatment of patients with bacterial keratitis was as effective as local instillation of the same drugs (12). Thermovibration massage at 10 Hz was a useful adjunct in combined treatment of patients with chronic cholecystitis and opisthorchiasis, improving motor-evacuation function of the biliary system (11).

InfraMed, a medical equipment company in the Netherlands, advertised an infrasound device called the SonoMat that may be used to break up arterial blockages (uncertain because the language is apparently Dutch) (16).

Vibrotherapy sources used in medicine generate audible as well as infrasound frequencies (14). At least two hand-held vibrotherapy devices are currently advertised to the public. The Infracronic QGM Quantum device, developed out of scientific research in Beijing, China, is said to focus chi or life energy into patients' bodies and stimulate[s] relaxation and healing. It operates at 8 to 14 Hz, 70 dB, and is said to be "recognized by FDA as a 510k Therapeutic Massager" (10,15). The second device is the Nostrafon Infrasound Wave Massager from Novafon, which is said to provide a 2.25-in. deep massage using mixed-frequency sound waves (7). Such vibrotherapy devices are used for treating horses (76) and athletes (9). [The Chi infrasound device is said to calm race horses by stimulating production of alpha brain waves (8).] The HydroSonic Relaxation System delivers infrasound and other low-frequency sound to the body by water conduction through a heated water mattress. The treatments can be applied through clothing and casts and the low-frequency waves can be programmed to penetrate surface muscles and internal organs to massage deep tissue. Typical treatments last about 30 minutes. The frequencies are generated by a compact disc and amplified. Users are said to include physicians, trainers, physical therapists, chiropractors, and spas (77).

2.4 Industrial Sources

Infrasound exposure is not uncommon in the vicinity of operating heavy machinery. In a Finnish survey of industrial work sites, infrasound pressure levels usually ranged from 80 to 100 dB, significantly higher than in the vicinity of the workplace. Highest infrasound levels were produced by blowers, pumps, oil burners, air compressors, drying towers, and heavy rotating machinery. The highest level (127 dB) was measured 100 m from a crusher at a mine (5).

2.5 Nonlethal Weapons

The U.S. Army has an infrasound weapons program, and infrasound is being considered for riot control and other police actions. [Little evidence was found that infrasound weapons are currently used beyond testing.] The use of infrasound-generating nonlethal weapons is based on the assumption that high-power infrasound will incapacitate those subjected to it with nausea and other gastrointestinal disturbances. Transmission of infrasound energy through the air is not

as efficient as transmission through mechanical vibrations at infrasound frequencies. One argument against the feasibility of the use of infrasound in nonlethal weapons is that infrasound's wavelengths (17 m and above) are so long that they spread out too rapidly to be focused (19). A device that can aim parametric infrasound without affecting the user could generate infrasound by mixing two ultrasonic acoustic waves (20). Such a method has been tested in Great Britain. Other infrasound-generation devices may have been used for riot control in Northern Ireland (18).

2.6 Other Sources

Other sources include explosions, bridge vibration, and air heating and cooling equipment (1). Infrasound sound pressure levels of predominantly single frequencies (i.e. tones) were low under a bridge, inside an automobile, and beside a cooling tower. Sound pressure levels were also low beside a refrigerator and inside a computer room. A washing machine in the spin cycle (dehydration process) emitted infrasound at 81 dB. Wooden houses have higher sound pressure levels (highest level > 100 dB) than concrete structures (17).

3.0 Regulations and Criteria

A search of several *Code of Federal Regulations* titles and recent reviews indicated that there are no U.S. or international regulations for permissible exposure limits for infrasound exposure. OSHA (21) in 29 CFR 1926.52, Occupational noise exposure, provides limits based on length of exposure to sound pressure levels of 90 to 115 dBA slow response (eight hours down to 15 minutes or less).

The American Conference of Governmental Industrial Hygienists (ACGIH) recommends that except for impulsive sound with durations of less than two seconds, one-third octave levels for frequencies between 1 and 80 Hz should not exceed a SPL ceiling limit of 145 dB and the overall unweighted SPL should not exceed a SPL ceiling limit of 150 dB; no time limits are specified for these recommended levels (22). Under its occupational guidelines for infrasound exposure, the New Zealand Occupational Safety and Health Service recommended using guidance for safe infrasound exposure given by von Gierke and Nixon (78) and Woodson (79) (both references cited by 80). NASA (23) established criteria for noise exposure applicable to space craft and space stations. The infrasonic, long-term annoyance noise exposure requirements stated that the infrasound sound pressure level in natural and induced environments SHALL be less than 120 dB in the frequency range 1 to 16 Hz for 24-hour exposure. WHO (74) and U.S. EPA (81) did not give any guidance for an upper limit to infrasound exposure.

The "therapeutic" infrasound devices would be subject to regulation by FDA under the Federal Food Drug and Cosmetic act as products meeting the definition of electronic product radiation. According to Section 532 of the Act "the term 'electronic product radiation' means...any sonic, infrasonic, or ultrasonic wave, which is emitted from an electronic product as the result of the operation of an electronic circuit in such product". 21CFR1000.15 (82) lists "Examples of electronic products subject to the Radiation Control for Health and Safety Act of 1968" and includes infrasonic vibrators as "examples of electronic products which may emit infrasonic, sonic, and ultrasonic vibrations resulting from operation of an electronic circuit". No

performance standards for infrasonic radiation-emitting products are included in 21CFR Part 1050.

4.0 Toxicological Data

The literature search identified 69 studies, 34 of which are in English. Twenty-four of the identified human studies are included in the annotated bibliography. Of these, references for 6 citations have been retrieved. English abstracts are available for 15 citations.

This section briefly describes studies reported in the open literature relating to physiological and psychological, but not necessarily adverse, effects resulting from exposure to infrasound frequencies. Where a substantial number of reported studies were identified, the information is presented in the form of an annotated bibliography. For studies in animals, all identified studies are described. For human studies, only selected studies judged to be particularly relevant after a limited review are included. The selection of human studies for inclusion was based primarily on availability of the article or abstract in English. References considered for human data but not annotated here are listed in section 7.0.

4.1 General Toxicology

4.1.1 Human Studies

General

Broner, N. 1978. The effects of low frequency noise on people—A review. *J. Sound Vib.* 58(4):483-500. (Ref. No. 26)

This paper presents very brief summaries of human studies (the majority of very short duration). "A review of the effects of low frequency noise indicates that the effects are similar to those of higher frequency noise, that the noise in the 20-100 Hz range is much more significant than infrasound at similar sound pressure levels and that the possible danger due to infrasound has been much over-rated." The primary effect of infrasound appears to be annoyance. Aural pain and damage (i.e., scarring of the tympanic membrane and vascular infection of the eardrum membrane) have been reported. Pressure sensation in the middle ear is a consistent finding (beginning at 127-133 dB). There is no valid research basis for claims on the use of infrasound as a weapon (e.g., use for riot control and non-violent crowd dispersal weapon claims).

Burt, T. 1996. Sick building syndrome: The acoustic environment. NO 10217. *Indoor Air '96*, Proceedings of the 7th International Conference on Indoor Air Quality and Climate held July 21-26, 1996, in Nagoya, Japan. Vol. 1, pp. 1025-1030. Available under "References—Part 2" at <http://users.iafrica.com/s/sa/salbu/apollo/apollo2.html>. Last accessed on September 6, 2001. (Ref. No. 83)

A low-frequency noise of ~7 Hz occurring in several office rooms produced symptoms in individuals typical of sick building syndrome, demonstrating that the low-frequency component of ventilation noise can be amplified in tightly sealed rooms. It was proposed that repeated or long-term exposure could be "triggering an allergic-type response."

Kuralesin, N.A. 1997. Health related and medico-biological aspects of the effects of infrasound. *Noise Vib. Bull.* (Reprinted from *Meditsina Truda I Promyshlennaya Ekologiya*, No. 5):221-226. NIOSHTIC record 1998:55553. (Ref. No. 84)

There is no agreement for the biological activity of infrasound. The vascular reaction of the middle ear and hearing sensitivity have been found to increase with increasing infrasound frequency, whereas vestibular and subjective indicators and central nervous system reaction have been found to increase with decreasing frequency. Analysis of the regression curves of the effects indicated that biological action of infrasound on humans can range from "unclear, abraded forms" to death. An association between infrasound exposure and a "hypothalamic crisis with sensory/somatovegetative visceral symptoms" was suggested.

Kawano, A., H. Yamaguchi, and S. Funasaka. 1991. Effects of infrasound on humans: A questionnaire survey of 145 drivers of long distance transport trucks. *Pract. Otol. Kyoto* 84(9):1315-1324. (Japanese) BIOSIS record 1992:99639. (Ref. No. 30)

Drivers of long distance transport trucks exposed to infrasound at about 115 dBA had no statistically significant incidence of fatigue, yawning, sleepiness, vertigo, tinnitus, headache, subdued sensation, hearing impairment, abdominal symptoms, or hypertension when analyzed with respect to exposure, work hours, driving hours, and rest hours. "Exposure to about 115 dBA of infrasound has no effect on humans."

Radneva, R. 1997. Studying the effect of acoustic conditions in the living environment of multifamily buildings on inhabitants. *Khig. Zdraveopazvane* 40 (3-4):40-44. (Bulgarian) EMBASE record 1998252323. (Ref. No. 85)

Studies of 1063 residents in multifamily buildings in Sofia, Bulgaria, experiencing noise level above 60 dBA and infrasound levels from 55 to 78 dB found a statistically significantly increased percentage of persons with psychosomatic complaints (e.g., weakness and fatigue) and sleep disturbance (e.g., restlessness during sleep) versus those exposed to lower level noise and infrasound.

Experimental Studies

Andresen, J., and H. Moller. 1984. Equal annoyance contours for infrasonic frequencies. *J. Low Freq. Noise Vib.* 3(3):1-9. EMBASE record 85169104. (Ref. No. 24)

Eighteen subjects (18 to 25 years old) exposed to four infrasonic frequencies at various intensity levels (both not provided in abstract) for 15 minutes (one stimulus per day) rated the annoyance to each stimulus. Equal annoyance curves showed that to achieve a given amount of annoyance, low frequencies required greater sound pressure and suggested that small changes in the latter parameter could cause significantly large changes in annoyance in the infrasonic region. A weighting curve with a slope of 12 dB/octave was proposed for the assessment of annoyance and loudness for infrasound, while 95 dB was proposed as the maximum permitted level for environmental purposes.

Borredon, P., and J. Nathi. 1973. Physiological reactions of human subjects exposed to infrasounds. *Rev. Med. Aeronaut. Spat.* 12(46):276-279. (French) EMBASE record 74130187. (Ref. No. 85)

Young males (n=42; 19 to 23 years old) were exposed to mechanical sinusoid air vibrations of 7.5 Hz and 130 dB for 50 minutes. A small but significant increase in blood pressure was observed.

Danielsson, A., and U. Landstrom. 1985. Blood pressure changes in man during infrasonic exposure. An experimental study. *Acta Med. Scand.* 217(5):531-535. MEDLINE record 85275572. (Ref. No. 31)

Twenty healthy males (20 to 30 years old) were exposed to frequencies of 6, 12, and 16 Hz at pressure levels of 95, 110, and 125 dB for 20 minutes in one series of experiments and then for one hour with random exposure of infrasound (125 dB/16 Hz) or low-grade frequency noise (50 dB/50 Hz) on alternate days in a second series of experiments. Infrasound (at all tested frequencies) was observed to increase diastolic blood pressure—the most significant effect was seen with 16 Hz, and the maximum mean increase of 8 mm Hg occurred after 30 minutes—and decrease systolic blood pressure and pulse rate, suggesting that a peripheral vasoconstriction with increased blood pressure was induced with acute infrasound stimulation.

Harris, C.S., and D.L. Johnson. 1978. Effects of infrasound on cognitive performance. *Aviat. Space Environ. Med.* 49(4):582-586. MEDLINE record 78144181. (Ref. No. 34)

In several experiments to assess cognitive performance during exposure to infrasound and noise, no reduction in performance was observed. In addition, no dizziness or disorientation was reported, which led the authors to conclude that "adverse effects of infrasound have been exaggerated." The experiments consisted of a Serial Search Task where volunteers were exposed for 15 minutes to 65 dB ambient noise (AN), a low-frequency background noise (BN) at 110 dB, a 7-Hz tone at 125 dB plus AN, and a 125-dB tone plus BN; a Complex Counting Task where subjects were exposed to the same conditions but for 30 minutes; and again the Complex Counting Task, in which exposure was for 15 minutes to BN and 7-Hz tones at 125, 132, and 142 dB plus BN.

Ising, H. 1980. Psychological, ergonomical, and physiological effects of long-term exposure to infrasound and audiosound. *Noise Vib. Bull.* [volume and number not provided]:168-174. NIOSHTIC record 1997:64651. (Ref. No. 87)

When subjects were exposed to 3 to 6 Hz, 6 to 12 Hz, or 12 to 24 Hz at 110 dB or a combination of 6 to 12 Hz tones with motorcycle race noise (500-2000 Hz at 75 dB), stress effects of low frequency sounds were smaller than those of higher frequency noise. Psychological tensions and loss of concentration were increased as the sound frequencies increased. In contrast, reaction time, respiration, and heart rate were not affected by the exposure.

Johnson, D.L. 1982. Hearing hazards associated with infrasound. In: Hamernik, R.P., D. Henderson, and R. Salvi, Eds. *New Perspectives on Noise-Induced Hearing Loss*. Raven Press, New York, NY, pp. 407-421. (Ref. No. 27)

This review summarizes several studies with infrasound conducted in humans (Table 2 in paper) and animals. (Note: data were limited up to 1982.) Evaluation of the human data resulted in the following conclusions: continuous exposures to infrasound below 140 dB (for less than 30

minutes) do not cause temporary threshold shift (TTS) of auditory acuity; exposures at high levels and of short duration (i.e., five minutes or less) do not cause TTS; and, TTS occurs at frequencies >1000 Hz. Therefore, levels of continuous infrasound for short periods are believed to be "safe" if below 150 dB, while exposures up to 24 hours are believed to be "safe" if at or below 118 dB. Impulse-type infrasound was judged to be definitely safe below 150 dB and possibly safe at higher levels.

Karpova, N.I., S.V. Alekseev, V.N. Erokhin, E.N. Kadyskina, and O.V. Reutov. 1970. Early response of the organism to low-frequency acoustic oscillations. *Noise Vib. Bull.* 11(65):100-103. NIOSHTIC record 1997:59793. (Ref. No. 29)

When male volunteers were exposed to simulated industrial infrasound of 5 and 10 Hz and levels of 100 and 135 dB for 15 minutes, feeling of fatigue, apathy, and depression, pressure in the ears, loss of concentration, drowsiness, and vibration of internal organs were reported. In addition, effects were found in the central nervous system, the cardiovascular system, and the respiratory system. Synchronization phenomena were enhanced in the left hemisphere. Visual motor responses to stimuli were prolonged, and the strength of effector response was reduced. Heart rate was increased during the initial minutes of exposure. Depression of the encephalic hemodynamics with decreased venous flow from the skull cavity and was observed. Heart muscle contraction strength was reduced. Respiration rate was significantly reduced after the first minute of exposure.

Landstrom, U., and M. Bystrom. 1984. Infrasonic threshold levels of physiological effects. *J. Low Freq. Noise Vib.* 3(4):167-173. EMBASE record 85174229. (Ref. No. 28)

Exposure to 6 and 16 Hz at levels 10 dB above the hearing threshold was associated with a reduction in wakefulness.

Lidstrom, I.M. et al. 1978. The effects of ultrasound on humans. *Invest. Rep. (Umea University, Sweden)* 33:1-42. (Swedish) NIOSHTIC record 1997:71512. (Ref. No. 32)

The effects of long-term exposure to infrasound were studied in 40 active Swiss airforce pilots who were exposed to a frequency of 14 or 16 Hz at 125 dB. Somatic and psychic functions were affected in the following ways: blood pressure was decreased causing deterioration of blood suffusion of vital organs; heart rate and blood pressure were increased during psychological tests; alertness was decreased; the electrical resistance of the skin was decreased more quickly versus unexposed individuals; and hearing threshold and time perception were altered.

Mohr, G.C., J.N. Cole, E. Guild, and H.E. Gierke. 1965. Effects of low frequency and infrasonic noise on man. *Aerosp. Med.* 36(9):817-824. NIOSHTIC record 1997:3235. (Ref. No. 88)

Five noise-experienced Air Force officers (4 males, 1 female; 24 to 46 years old) were exposed for up to two minutes to high-intensity broad-band, narrow-band, and pure-tone low-frequency noise (sources: turbojet engine, Thermal Structures Tunnel, RTD Low-Frequency Siren, AMRL High-Intensity Noise Chamber, and NASA-LRC Low-Frequency Noise Facility) to assess human tolerance to the noises produced during the launching of spacecrafts. Exposures to low-frequency noise up to 150 dB were observed to be within human tolerance limits. General symptoms reported by the officers exposed to infrasound were minor chest wall and body hair

vibration and changes in respiratory action; visual acuity, spatial orientation, and hand coordination were subjectively normal.

Moller, H. 1984. Physiological and psychological effects of infrasound on humans. *J. Low Freq. Noise Vib.* 3(1):1-16. EMBASE record 85067664. (Ref. No. 25)

Sixteen subjects exposed for three hours to inaudible infrasound and audible infrasound reported annoyance and a feeling of pressure on the ear at <20 dB above the hearing threshold. No effects on the cardiovascular system and no significant deterioration in performance were observed. At levels below the hearing threshold, no effects were seen.

Okada, S. 1990. Study on the measurement of infrasound and perceptible response to infrasound in life environment. *Jpn. J. Health Hum. Ecol.* 56(5):236-250. (Japanese) TOXLINE record 1991:151218. [See also Tsunekawa et al., 1987.] (Ref. No. 89)

Sound pressure levels were measured and human perception were studied at various places such as under a bridge, inside an automobile, and beside a cooling tower. The following 50% response levels of total response were found: 102 dB at 6 Hz, 93 dB at 10 Hz, 92 dB at 13 Hz, 85 dB at 20 Hz. The 20% response level was 6 dB lower than the threshold value, and the 80% response level was 6 dB higher.

Okada, A., and R. Inaba. 1990. Comparative study of the effects of infrasound and low-frequency sound with those of audible sound on sleep. *Environ. Int.* 16(4-6):483-490. (Ref. No.90)

When 18 healthy male students (20 to 25 years old) were exposed to infrasound and low-frequency sound (10, 20, 40, and 60 Hz) during sleep, the pattern of sleep was little affected. In contrast, audible sound (i.e., synthesized traffic noise [25-1600 Hz at 40, 50, and 60 dB]) had more "harmful effects" on sleep (e.g., caused difficulty in initiating sleep and affected reaction rates after exposure).

Okamoto, K., A. Yoshida, J. Inoue, and H. Takyu. 1986. The influence of infrasound upon human body. *Sangyo Ika Daigaku Zasshi* 8(Suppl.):135-149. (Japanese) (Ref. No. 33)

Subjects were exposed to infrasound at 10 and 15 Hz via whole-body exposure, whole-body exposure with an ear plug, and by head phone. The hearing threshold was significantly increased with whole-body exposure with an ear plug but was not significantly different between the other stimulations. Body sway and individual variability was greater at 15 Hz than at 10 Hz. Nystagmus was not observed, nor were any changes in respiration, pulse, blood pressure, ECG, ENG, GSR, and OKN.

Slarve, R.N., and D.L. Johnson. 1975. Human whole-body exposure to infrasound. *Aviat. Space Environ. Med.* 46(4):428-431. (Ref. No. 91)

Four male volunteers (college age) were exposed to infrasound frequencies ranging from 1 to 20 Hz at levels of 120 to 144 dB for eight minutes. All reported painless pressure build-up in the middle ear and experienced body vibration and voice modulation. There were no significant

changes in these observations as well as in objective measurements (i.e., heart and respiration rates).

Strandberg, U.D., P. Bjerle, A. Danielsson, S. Hornqwist-Bylund, and U. Landstrom. 1986. *Studies of Circulation Changes During Exposure to Infrasound*. Arbetarskyddsstyrelsen, Publikationsservice, Solna, Sweden, 29 pp. (Swedish) TOXLINE record 1988:73119. (Ref. No. 92)

Eleven healthy subjects exposed to infrasound at 16 Hz at 125 dB in a specially prepared pressure chamber for one hour had an increased diastolic blood pressure and a decreased systolic blood pressure. In addition, pulse rate was increased. There were no effects on peripheral and deep circulation.

Taenaka, K. 1989. A study on the effect of infrasound. *J. Oto-Rhino-Laryngol. Soc. Jpn.* 92(9):1399-1415. (Japanese) MEDLINE record 90063971. (Ref. No. 35)

Subjects exposed to infrasound at 10 to 15 Hz and 130 to 135 dB for 30 minutes experienced no changes in hearing level, vestibular functions, and autonomic nervous functions. [Noted: an experimental study using guinea pigs was also conducted; study details and results are presented in the abstract.]

Takigawa, H., F. Hayashi, S. Sugiura, and H. Sakamoto. 1988. Effects of infrasound on human body sway. *J. Low Freq. Noise Vib.* 7(2):66-73. EMBASE record 89075091. (Ref. No. 36)

Healthy males (n=34; ages not provided) exposed to 5 and 16 Hz at 95 dB for five minutes inhibited the temporary confusion of the mode of body sway experienced at the time of switchover from opening to closing of the eyes, suggesting the acceleration of vestibulum excitability upon exposure to infrasound. No effects occurred with exposure to noise.

Tsunekawa, S., Y. Kajikawa, S. Nohara, M. Ariizumi, and A. Okada. 1987. Study on the perceptible level for infrasound. *J. Sound Vib.* 112(1):15-22. BIOSIS record 1987:173665. [See also Okada, 1990.] (Ref. No. 93)

A field survey studying the human perception of infrasound (6 to 23 Hz) at places such as under a bridge, inside an automobile, and around a cooling tower reported a threshold value (50% response level) at 10 Hz of about 93 to 94 dB. The 20% response level was nearly 6 dB lower than the threshold value, while the 80% response level was almost 6 dB higher than the threshold value. For the chest and abdomen, the response level was 6 to 9 dB higher than that of the total response for the ear, head, chest, and abdomen.

4.1.2 Animal Studies: Acute Exposure Duration

Citations for 32 acute animal studies are annotated in this section; 12 of the references have been retrieved and are available in English. English abstracts are available for an additional five references.

Acute exposure duration for the purpose of inclusion in this section is defined as <24 hours. Several studies in subsection 4.1.3 (Short-term Exposure duration) also include acute exposure duration experiments.

Studies in Rats

Alekseev, S.V., E.N. Kadyskina, N.T. Svistunov, L.I. Alekseeva, E.A. Bukharin, and L.I. Kalinina. 1980. Some biochemical aspects of the mechanism of action of infrasonic oscillations on the body. *Gig. Tr. Prof. Zabol.* (4):21-24. (Russian) BIOSIS record 1981:299259. (Ref. No. [37](#))

Rats exposed to infrasonic oscillations for 15, 30, and 60 min showed frequency-dependent phasic changes in cholinergic activity as determined by measurements of acetylcholine and acetylcholinesterase.

Alekseev, S.V., V.V. Glinchikov, and A.S. Nekhoroshev. 1991. Reactive changes in the myocardium following exposure to low-frequency infrasonic acoustic vibrations. *Kosm. Biol. Aviakosm. Med.* 25(1):49-51. (Russian) BIOSIS record 1991:303461 (no abstract). (Ref. No. [94](#))

[See similar studies by these authors on rats and guinea pigs.]

Guo-You, F., C. Jing-Zao, and J. Ke-Yong. 1999. Changes of glutamate in brain of rats exposed to infrasound. *J. Fourth Mil. Med. Univ.* 20(4):288-290. (English) LIFESCI record 1999:102062. (Ref. No. [38](#))

Brain injury observed in rats exposed to infrasound at high sound pressures may be due to elevated glutamate concentrations and its exciting toxicity. Four groups of rats were exposed to 8 Hz or 16 Hz at 90 dB or 120 dB for 2 hours. Significant increases in brain glutamate were observed in rats exposed at 120 dB, with the effect being more pronounced in the rats exposed to 16 Hz.

Nekhoroshev, A.S. 1998. Studying some mechanisms underlying effects of low-frequency acoustic vibrations. *Med. Tr. Prom. Ekol.* (5):26-30. (Russian) MEDLINE record 1998327434. (Ref. No. [95](#))

Experimental data from rats and guinea pigs exposed to infrasound indicate four zones of response of hearing and the vestibular apparatus, with infrasound directly affecting nuclei of cranial nerves VIII and X. Apparently, infrasound indirectly affects other organs and systems that are functionally linked to the vagus nerve.

Nishimura, K. 1988. The effects of infrasound on pituitary adrenocortical response and gastric microcirculation in rats. *J. Low Freq. Noise Vib.* 7(1):20-33. (Ref. No. [41](#))

Infrasound exposure may influence the endocrine system and autonomic nervous system according to studies in which rats were exposed to infrasound for 20 minutes. Changes in pituitary adrenocortical response, as measured by changes in plasma ACTH and corticosterone,

paralleled those observed in humans but occurred about 30 dB above the human threshold of sensation. The frequency characteristics of the responses of the rat pituitary adrenocortical system corresponded to about 80 phon on the equal-loudness curves. Rats exposed to 16 Hz at 120 dB for 20 minutes showed a significant reduction (19.1%) in gastric mucosal blood flow from pre-exposure levels. The reduction was significantly less after 10 minutes of exposure and at 10 minutes post exposure.

Petounis, A., C. Spyrakis, and D. Varonos. 1977a. Effects of infrasound on the conditioned avoidance response. *Physiol. Behav.* 18(1):147-151. MEDLINE record 78068875. [Reference attached] (Ref. No. 44)

Performance decrements were observed in rats (20/group) in acquisition of a conditioned avoidance response during exposure to infrasound (2 Hz) at 104 dB and in retention 24 hours later. Light or sound was used as the conditioned stimulus during the acquisition phase with infrasound exposure. The decrements were more pronounced when sound was the conditioned stimulus. The retarding action on cortical arousal was similar to that of depressant drugs.

Petounis, A., C. Spyrakis, and D. Varonos. 1977b. Effects of infrasound on activity levels of rats. *Physiol. Behav.* 18(1):153-155. MEDLINE record 78012628 (no abstract). [Reference attached] (Ref. No. 96)

Female rats (20/group) exposed to infrasound (2 Hz at 105 dB, 7 Hz at 122 dB, and 16 Hz at 124 dB) for up to 2 hours showed significant decreases in spontaneous activity levels and exploratory behavior: 55% (7 Hz) to 100% (2 Hz) of the rats were asleep within 50 to 60 min compared to only 15% of control rats after 90 minutes. The infrasound-generating apparatus is described in detail.

Spyrakis, C., Z. Papadopoulou-Daifoti, and A. Petounis. 1978. Norepinephrine levels in rat brain after infrasound exposure. *Physiol. Behav.* 21(3):447-448. MEDLINE record 79116491 (no abstract). [Reference attached] (Ref. No. 40)

When Wistar rats (12-13/group) were exposed to 2 Hz at 105 dB, 7 Hz at 122 dB, and 16 Hz at 124 dB for 1 hour immediately before sacrifice, those exposed to 7 Hz and 16 Hz at 122-124 dB showed significantly decreased brain norepinephrine concentrations.

Spyrakis, C., Z. Papadopoulou, B. Zis, and D. Varonos. 1980. Effects of diazepam-infrasounds combination on locomotor activity and avoidance behavior. *Pharmacol. Biochem. Behav.* 12(5):767-771. MEDLINE abstract 80234900. [Reference attached] (Ref. No. 39)

Rats retained a conditioned-avoidance behavior better than controls when treated with diazepam [an anxiolytic and muscle relaxant drug], but motor activity was increased and retention was decreased when the diazepam-treated rats were exposed to infrasound. Brain homogenate concentrations of norepinephrine and dopamine were slightly affected in both cases. While rats exposed to infrasound alone showed significantly decreased norepinephrine concentrations, infrasound plus diazepam exposure significantly increased norepinephrine levels in brain homogenate. The combination induced a significant decrease in brain dopamine as did infrasound exposure alone.

Svidovyi, V.I. 1987. Mechanism of perception and effect on infrasound on the bodies of experimental animals and man. *Gig. Sanit.* (3):88-89. (Russian) MEDLINE record 87192148 (no abstract). [Reference attached] (Ref. No. 42)

Rats were exposed to 8 Hz at 120 dB for 0.5 hour (group 3), 1 hour (group 1), or 6 hours (group 2). The rats were injected intraperitoneally with a 0.005% solution of neutral red in Hank's solution and sacrificed after 0.5 hour. The isolated organs of the animals in group 3 were placed in a neutral red solution for 0.5 hour while exposed to the infrasound treatment. The optical densities of the alcoholic extracts of the spleen and brain of group 2 were significantly elevated (1.22- and 1.25-fold, $p < 0.05$). No significant differences were seen for extracts from the liver and kidneys in group 2. No significant differences were observed for the rats of group 1 in any organs. The membranes of isolated organs of group 3 exhibited much greater absorptive capacity for the dye as determined from the optical densities of their alcoholic extracts. All organs showed significantly enhanced ($p < 0.05$) membrane permeability with increases of 3.6-fold for liver, 3.2-fold for kidney, 3.5-fold for spleen, and 2.7-fold for brain.

Yamamura, K., and R. Kishi. 1980. Effects of infrasound on the Rota-Rod Treadmill performance of rats. *Europ. J. Appl. Physiol. Occup. Physiol.* 45(1):81-86. MEDLINE record 81044095. (Ref. No. 43)

Rats that had shown superior performance on the Rota-Rod Treadmill were not affected by 70-minute exposure to infrasound of 16 Hz at 105 dB whereas the group of rats who were poor performers on the treadmill showed reduced endurance when exposed to 16 Hz at 105 dB for 10 minutes, to 16 Hz at 95 dB for 70 minutes, and to 16 Hz at 85 dB for 150 minutes.

Studies in Mice

Busnel, R.G., and A.G. Lehmann. 1977. Synergistic effects of infrasonic noise and ethanol on measurable behavior. *Compt. Rend. D. Sci. Nat.* 285(4):423-425. (French) MEDLINE record 78022729 (no abstract). (Ref. No. 46)

Infrasound plus ethanol exposure affected time to fatigue of mice subjected to forced-swimming tests. [See Lehman and Bushnel (1979) for details of a similar study.]

Busnel, R.G., and A.G. Lehmann. 1978a. Infrasound and sound: Differentiation of their psychophysiological effects through use of genetically deaf animals. *J. Acoust. Soc. Am.* 63(3):974-977. (English) MEDLINE record 78218878. [Reference attached] (Ref. No. 45)

Two strains of mice with normal hearing exposed to high-frequency sound (500 to 10,000 Hz) showed reduced resistance to fatigue as determined by a 25 to 50% decrease in forced swimming time (time to submersion), whereas deaf mice were unaffected. However, exposure to low-frequency sounds of 6 to 50 Hz with a threshold of 115 to 160 dB reduced swimming time in both hearing and deaf mice.

Busnel, R.G., and A.G. Lehmann. 1978b. Suppression by ascorbic acid of neuromuscular fatigue due to sound-alcohol synergy. *Compt. Rend. D. Sci. Nat.* 287(4):373-374. (French) MEDLINE record 79064076 (no abstract). (Ref. No. 69)

The protective effect of ascorbic acid against neuromuscular fatigue of swimming mice while under the influence of alcohol and infrasound was attributed to acetaldehyde detoxification.

Kosaka, T., and S. Yamada. 1984. Research note: Effects of low frequency noise on mice. *J. Low Freq. Noise Vib.* 3(3):17-19. EMBASE record 85169106. [Reference attached] (Ref. No. 97)

This note reported that wild mice appeared to have left areas in Japan near expressway bridges. Infrasound measurements indicated that the dominant [low] frequencies of the traffic noise were 2 to 3 Hz and 10 to 20 Hz at a peak sound pressure level of 105 dB. The authors report the results of two laboratory studies. After training mice to respond to sound (conditioned reflex) by moving from one cage to another, it was determined that the animals could not detect sounds of less than 1000Hz (test range = 100Hz – 8000 Hz). In a second study, two groups of mice (n = 8 or 7) were exposed 10 hours a day for 100 days (1/2 their lifespan) to either 16 Hz at 120 dB or 60 dB. No differences between the groups were observed in consumption of food or water or body weight gain. At the end of the experiment two animals from the group exposed at 120dB were necropsied. There were not observable abnormalities. It was concluded that low frequency sound had no physical effects on the mice, but may indirectly cause mental effects.

Lehmann, A.G., and R.G. Busnel. 1979. Reduction of swimming time in mice through interaction of infrasound and alcohol. *Psychopharmacology* 65(1):79-84. (English) MEDLINE record 80057421. [Reference attached] (Ref. No. 47)

Muscular fatigue, as measured by time to submersion during a forced-swimming test, was enhanced by exposing mice for 2 hours before the test to infrasound of fixed frequency and intensity (6, 10, and 15 Hz at 106 dB) [the authors included 30 and 50 Hz at 100 dB in the infrasound range] plus oral doses of ethanol from 0.5 to 3.5 hours before the test. The effects of alcohol and infrasound together were more than additive and were prolonged for more than 2 hours after alcohol clearance from the blood. Blood alcohol levels reached concentrations associated with psychophysical impairment for only 15 minutes. Nonauditory pathways were probably involved since both genetically deaf mice and mice with normal hearing were affected similarly.

Studies in Guinea Pigs

Balabanov, A.A., M.Z. Beigel', M.Kh. Zelikman, Yu.V. Portnoi, and B.M. Stepanov. 1980. Reaction of guinea pigs to infrasonic vibration velocity. *Biofizika* 25(2):323-325. (Russian) MEDLINE record 80175620 (no abstract). (Ref. No. 98)

The study, according to the MEDLINE index terms determined stress in guinea pigs exposed to infrasonic vibrations by measuring their galvanic skin responses.

Hiraide, F. 1985. Effects of infrasound on the ear. *Oto-Rhino-Laryngol. Tokyo* 28(4):23-29. (Japanese) EMBASE record 85215583. (Ref. No. 49)

Guinea pigs (34) exposed to infrasound (1, 10, or 20 Hz) at 120-163 dB SPL (sound pressure level) for 1 hour did not exhibit any nystagmus or balance disturbances. After sacrifice on day 14 post exposure, cochlear damage, but no damage to the tympanic membrane or middle ear, was observed in guinea pigs exposed to 20 Hz at 163 dB SPL. Examination by scanning electron microscope revealed hair cell damage and globus formation of the tectorial membrane in the apical turn of the cochlea. The globus disturbed the attachment of sensory hairs to the undersurface of the tectorial membrane. The numbers of ears with pathology increased with increasing sound intensity, but levels below 133 dB SPL for 1 hour did not induce morphological changes in the guinea pig cochlea.

Hiraide, F., et al. [sic] 1987. Effects of infrasound on the ear: Light microscopic observation. *Oto-Rhino-Laryngol.* Tokyo 30(4):11-15. (Japanese) BIOSIS record 1988:183749. (Ref. No. 48)

This study repeated the same exposure conditions used in the Hiraide (1985) experiment. No morphological damage was seen in other guinea pig ear structures (spiral and vestibular ganglion cells, cochlear and vestibular nerves, saccule, utricle, and semicircular canals). The threshold for morphological changes was 140dB.

Parker, D.E., L.A. Ritz, R.L. Tubbs, and D.L. Wood. 1976. Effects of sound on the vestibular system. (Final report) AMRL-TR-75-89; NTIS order no. AD-A025 969/7. NTIS record 1976(17):73. (Ref. No. 99)

Guinea pigs, monkeys, and humans were subjects of studies of vestibular responses to audiofrequencies as well as to infrasound frequencies. No experimental details or results were given in the abstract.

Salt, A.N., and J.E. DeMott. 1998. Cochlear responses to infrasound in the 0.1 to 20 Hz range. Poster abstract from <http://www.aro.org/archives/1998/757.html>. Association for Research in Otolaryngology web site, last visited 9/3/01. (Ref. No. 51)

The guinea pig cochlea is highly sensitive to fluctuating infrasound stimulation (up to 20 Hz) of the inner ear fluids. Change in endonuclear potential (EP) was enhanced by perforating the otic capsule to produce a perilymph fistula.

Salt, A.N., and J.E. DeMott. 1999. Longitudinal endolymph movements and endocochlear potential changes induced by stimulation of infrasonic frequencies. *J. Acoust. Soc. Am.* 106(2):847-856. MEDLINE record 1999392049. [Reference attached] (Ref. No. 50)

Guinea pigs exposed to infrasound, via direct contact of the perilymph of the cochlear scala tympani or scala vestibuli with a fluid-filled pipette, exhibited large changes in EP, especially at about 1 Hz. Under some conditions, the EP changes exceeded 20 mV pk/pk in amplitude and were equivalent to a cochlear microphonic response. Cyclical, longitudinal endolymph displacement accompanied the EP changes.

Yoshida, A., and R. Nagano. 1986. The influence of infrasound vibration upon cochlea. *Sangyo Ika Daigaku Zasshi.* 8(Suppl.):123-128. (Japanese) MEDLINE record 8626114. (Ref. No. 52)

Amplitude and latency time of the auditory evoked potential (AP) were measured by electrocochleogram in anesthetized white guinea pigs that had been exposed to sound (white noise at 100 dB SPL or 4 kHz pure tone at 115 dB SPL) for 2 hours or to infrasound (10 Hz or 15 Hz, amplitude 5 mm) for 4 or 6 hours separately or simultaneously with sound. Exposure to both 4 kHz pure tone and infrasound vibration with 10 Hz, and 15 Hz@ significantly reduced the AP amplitude. Exposure to infrasound at 15 Hz slightly prolonged the AP latency time. Reissner's membrane had collapsed in a few cochlea. When guinea pigs were exposed to infrasound (20 Hz) at 115 dB SPL from a loudspeaker for 3 hours in a free field, the amplitude and latency time of P1 in the auditory brain stem response were not remarkably different from measurements before the exposure.

Studies in Chinchillas

Lim, D.J., and W. Melnick. 1982. Changes in the Organ of Hearing Produced by Sound. (Final Report 1 Mar 77 - 1 May 80). Sponsored by the Air Force Aerospace Medical Research Lab., Wright-Patterson AFB, OH. AFAMRL-TR-80-127. NTIS Order No. AD-A118 003/3. NTIS record 1982(25):54. [Reference attached] (Ref. No. 100)

Details for the chinchilla study are the same as those reported by Lim et al. (1982).

Lim, D.J., D.E. Dunn, D.L. Johnson, and T.J. Moore. 1982. Trauma of the ear from infrasound. *Acta Oto-Laryngol.* 94(3-4):213-231. MEDLINE record 83070718. [Reference attached] (Ref. No. 53)

Pathologies observed in chinchillas exposed about 25 minutes to continuous or intermittent infrasound (1 Hz at 170 dB; 10 Hz at 150, 160, or 170 dB; or 20 Hz at 150, 160, or 163 dB SPL) included the following (percent of incidence induced by continuous exposure in parentheses):

- tympanic membrane perforation (100%)
- stapes subluxation
- bleeding from mucosa of the middle ear
- bleeding from the tensor tympani muscle
- blood in the cochlear scalae (73%)
- Reissner's membrane rupture
- endolymphatic (cochlear) hydrops (78%)
- saccular wall rupture (100%)
- hair cell damage (67%)

Although the highest intensity, 170 dB, induced the highest percentage of ears with damage, the percentage of ears with pathologies decreased with increasing infrasound frequency.

Studies in Rabbits

Bachurina, T.I. 1974. Effect of short-term infrasonic stimuli on the brain bioelectric activity. *Fiziol. Zh. SSSR Imeni I.M. Sechenova.* 40(4):491-498. (Russian) MEDLINE record 75022417 (no abstract). (Ref. No. 101)

Changes in rabbit brain activity during infrasound exposure were monitored by electroencephalography.

Sidorenko, E.I., M.Kh. Zelikman, and A.V. Kaplina. 1988. Changes in eye tissues exposed to local action of infrasound. *Oftalmol. Zh.* (2):109-111. (Russian) MEDLINE record 88288931 (no abstract). (Ref. No. 102)

The indexing provides no additional information except that the test animals were rabbits.

Sidorenko, E.I., S.A. Obruchov, A.A. Dreval, and A.P. Tumasian. 1996. Experimental study of morphologic changes in ocular tissue structures after exposure to infrasound pneumomassage. *Vest. Oftamol.* 112(3):17-19. (Russian) MEDLINE record 96413163. (Ref. No. 103)

The eyes of chinchillas and rabbits exposed for 10-minute sessions for 5 and 10 days to infrasound massage at 4 Hz, depth 0.5 [no units in abstract], and amplitude 0.1 kg/cm², exhibited no detrimental effects. The greatest changes were observed in various segments of the vascular coating.

Sudzilovskii, F.V., Yu.M. Zagorskii, V.M. Islent'ev, and T.Ya. Milovanova. 1974. State of some rabbit nervous system parts after exposure to infrasound. *Arkh. Anat. Gist. Embriol.* 66(6):31-35. (Russian) MEDLINE record 75163969 (no abstract); BIOSIS record 1975:132767 (no abstract). (Ref. No. 104)

MEDLINE indexing terminology included cytology of the brain, cerebellum, pons, ependyma, ganglia, spinal cord, and trigeminal nerve. BIOSIS indexing terms included ultramicroscopic anatomy, cardiovascular system - blood vessel pathology, and nervous system - pathology.

Studies in Monkeys

Swanson, D.C. 1999. Non-lethal acoustic weapons: Facts, fiction, and the future. NTAR 1999 Symposium. Abstract available at <http://www.unh.edu/orps/nonlethality/pub/abstracts/1999/swanson.html>. Last accessed 8/28/01. (Ref. No. 20)

Exposure to 1 to 5 Hz in a piston-driven hyperbaric chamber at high-pressure levels consistently caused monkeys to lose their balance. The statement was not attributed to a source in this brief abstract.

Studies in Dogs and Primates

Johnson, D.L. 1976. *Infrasound, Its sources and its effects on man.* Johnson, D.L. 1976. *Infrasound: Its Sources and Its Effects on Man.* AMRL-TR-76-17. Aerospace Medical Research Lab. Wright-Patterson AFB, OH. NTIS report no. AD-A032 401/2. NTIS record 1977(01):10899. [Reference attached] (Ref. No. 75)

The author reports full body exposures of a baboon, a monkey, and six dogs of various sizes; however, he only discusses the dog results to any extent. Animals (with and without anesthesia) were exposed to the occupational limit envelope for infrasound for an undisclosed period of time, assumed to be acute. The occupational limit allows frequencies of 0.5 to 8 Hz for exposures up to 172.5 dB. From 8 Hz to 30 Hz, there is a reduction in loudness from 172.5 to 158 dB. Unanesthetized animals showed no observable evidence of adverse effects. Animals only became excited when the conditions of the experiment were rapidly changed. In anesthetized animals, there was no change in EEG or respiration rates until an SPL of 166 dB was reached. From 166 to 172 dB, respiration rates declined until, at 172 dB, respiration actually ceased for the larger dogs, due to "artificial" ventilation effects caused by infrasound. One dog was exposed over a period of six weeks for a total of 14 hours at the operational limits. At the end of this period, the animal was necropsied. There was no evidence of any pathological changes.

Studies in Unidentified Species

Chauchard, P., and H. Mazoue. 1962. Specificity of action of aerial infrasound on the nerve centers. *J. Radiol. Electr.* 54:313. (French) MEDLINE record 62019744 (no abstract). (Ref. No. 105)

According to the MEDLINE index terms, this study involved observations of brain physiological reactions to vibrations from aerial infrasound exposure. The species was not indexed.

4.1.3 Animal Studies: Short-Term Exposure Duration

Twenty short-term studies have been annotated. Full articles in English are available for 8 of the references. Abstracts in English are available for 11 additional citations.

Short-term exposure duration for the purpose of inclusion in this section is defined as >24 hours. None of the studies identified involved exposures of sufficient duration to qualify as subchronic or chronic studies.

Studies in Rats

Alekseev, S.V., V.V. Glinchikov, and V.R. Usenko. 1985. Myocardial ischemia in rats exposed to infrasound. *Gig. Tr. Prof. Zabol.* (8):34-38. (Russian) MEDLINE record 84030061 (no abstract). [Reference attached] (Ref. No. 55)

Rats and guinea pigs (5 test animals, 2 controls per group) were exposed to infrasound (4 to 16 Hz) at 90 to 145 dB for 3 h/day for 45 days; and tissues were collected on days 5, 10, 15, 25, and 45 for pathomorphological examination. A single exposure to 4 to 10 Hz at 120 to 125 dB led to short-term arterial constriction and capillary dilatation in the myocardium. Prolonged exposure led to nuclear deformation, mitochondrial damage, and other pathologies. Effects were most marked after 10- to 15-Hz exposures at 135 to 145 dB. Regenerative changes were observed within 40 days after exposure. [Full details were not extracted from this Russian article because of time constraints and the specialized vocabulary.]

Alekseev, S.V., V.V. Glinchikov, and V.R. Usenko. 1987. Reaction of liver cells to infrasound. *NVB. Noise Vib. Bull.* (translated from *Gig. Tr. Prof. Zabol.*, September 1986). pp. 131-132. NIOSHTIC record 1997:139491. (Ref. No. 59)

Infrasound exposure damaged the nuclear apparatus, intracellular membrane, and mitochondria of rat hepatocytes *in vivo*. Infrasound (2, 4, 8, or 16 Hz) at 90 to 140 dB for 3 h/day for 40 days induced histopathological and morphological changes in hepatocytes from rats sacrificed on days 5 to 40. Infrasound (8 Hz) at 120 to 140 dB induced pathological changes in hepatocytes from the glandular parenchyma and sinusoids. Changes included the following:

- loss of contact between damaged cells
- rounded appearance of damaged cells
- deformed nuclei
- chromatin redistribution to the nuclear membrane
- increased cytoplasmic RNA content

- RNA became strongly basophilic
- diffusive reactive changes at 120 dB such as mitochondrial swelling, a marked increase in:
 - matrix density, and deformation of the cristae
 - appearance of myelin-type bodies by day 25
 - appearance of lipid granules by day 40

Infrasound of 8 and 16 Hz frequencies at 140 dB induced the most damage:

- strongly deformed nuclei
- zones of lysis of the endoplasmic reticulum in the cytoplasm followed by vacuole formation
- lipid granules in the cytoplasm with osmophilic inclusions

Colasante, D.A., F.C. Au, H.W. Sell, and R.R. Tyson. 1981. Prophylaxis of adhesions with low frequency sound. *Surg. Gynecol. Obst.* 153(3):357-359. MEDLINE record 81275239. BIOSIS record 1982:163528. (Ref. No. 106)

Exposure of Sprague-Dawley rats (about 30/group) with cecal crush injuries to high-intensity, low-frequency sound (values not given in the abstract) reduced adhesion formation from the 83% incidence in the control rats to 23% in the group exposed to infrasound for the full 12 days. Efficacy of the prophylactic effect, which was attributed to the induced micromotion of the abdominal organs, increased with increasing duration. The induced motion apparently inhibited formation of spanning fibers. The rats did not exhibit any side effects from the infrasound treatment.

Dadali, V.A., V.I. Svidovyi, V.G. Makarov, L.B. Gorkova, V.A. Kuleva, R.N. Pavlova, O.V. Tarasova, and V.M. Timofeeva. 1992. Effects of infrasound and protective effect of adaptogens in experimental animals. *Gig. Sanit.* (1):40-43. (Russian) MEDLINE record 92406047 (no abstract). [Reference attached] (Ref. No. 58)

Prolonged exposure (up to 60 days) of rats to 8 Hz at 100 dB led to significant biochemical and morphological changes in the blood and tissues. Dosing the rats with even small doses of imidazoles (ethimizole and T-5) provided a marked protective effect, acting on the antioxidant status of the body. In the experiments, male rats of no specific strain (10/group) were exposed to 8 Hz at 100 dB for 3 h/day for 2 months with and without dosing with ethimizole or T-5, which were also tested alone. The authors reported variable effects of the imidazoles on infrasound-induced changes in erythrocyte concentrations of catalase, malonic acid dialdehyde, and glutathione reductase and the plasma concentrations of alanine aminotransferase, aspartate aminotransferase, and ceruloplasmin. Infrasound exposure induced tissue changes (destructive and atrophic changes of a focal character without marked gross disturbances in the lungs, liver, and kidneys as well as foci of proliferation of stromal elements) that were moderated by the imidazoles. Only insignificant peribronchial infiltration was noted after dosing. Dystrophic changes in the liver, heart, kidneys, adrenals, and testicles were lowered to a minimum.

Gabovich, R.D., O.I. Shutenko, E.A. Krechkovskii, G.M. Shmuter, and L.A. Stechenko. 1979a. Effect of infrasound on bioenergetics processes, organ ultrastructural organization and on regulation processes. *Gig. Tr. Prof. Zabol.* (3):9-15. (Russian) MEDLINE record 79149272 (no abstract). [Reference attached] (Ref. No. 57)

Male rats (20/group) exposed 2 h/day for 4 months to 8 Hz at 90 dB (group 2), 115 dB (group 3), and 135 dB (group 4) showed the following changes:

- Groups 2-4 showed increasing activities of α -ketoglutarate dehydrogenase with increasing sound pressure.
- Group 4 showed a significant decrease in succinate dehydrogenase, with the other groups showing a decreasing trend.
- The myocardial content of ATP (adenosine triphosphate) and ADP showed a tendency to decrease; group 4 showed significant decreases in both.
- The AMP content in the myocardium showed significant increases in groups 3 and 4.
- Plasma corticosterone increases were significant in groups 3 and 4.
- Changes in the myocardial ultrastructure included changes in the fine structure of the endothelium and myocytes organelles and reduction in the capillary length in the microcirculatory bed.
- Pathology was marked at 115 and 135 dB, with 90 dB being the threshold level.

No significant changes were noted in alkaline phosphatase in the myocardium or epinephrine content in the adrenals.

Gabovich, R.D., O.I. Shutenko, I.P. Kozyarin, and I.P. Shvaiko. 1979b. Experimental effects of the combined exposure to infrasound and ultra high frequency electromagnetic fields. *Gig. Sanit.* 10:12-14. (Russian) NIOSHTIC record 1997:93000. (Ref. No. 61)

Combined exposure to ultrahigh-frequency (UHF) electromagnetic fields and infrasound potentiated the effects induced by each separately. Rats were exposed to UHF at 100 mW/cm², to infrasound (8 Hz) at 110 dB, or to both for 2 h/day for 10 weeks. Parameters studied were measured before exposure and at weeks 2, 6, and 10. All exposures delayed body-weight gain, with the delay from combined exposure being statistically significant. The following effects were observed after exposure to infrasound with and without UHF exposure:

- Increased working capacity at 2 weeks but decreased after 6 weeks, especially in rats subjected to the combined treatment.
- Increased oxygen requirements at 6 weeks, which returned to normal by 10 weeks.
- Increased summation subthreshold parameters (while UHF alone caused decreases)

All treatments significantly increased unconditioned reflexes by week 6, but only rats exposed to infrasound plus UHF showed increases at week 10. All treatments induced significant changes in immunological parameters as shown by decreases in basophil stability and development of autoallergic processes.

Gordeladze, A.S., V.V. Glinchikov, and V.R. Usenko. 1986. Experimental myocardial ischemia caused by infrasound. *Gig. Tr. Prof. Zabol.* (6):30-33. (Russian) MEDLINE record 86301946 (no abstract). [Reference attached] (Ref. No. 54)

Rats and guinea pigs (10 animals per group) were exposed to 8 Hz at 120 dB for 3 h/day for 1, 5, 10, 15, 25, or 40 days. Concentrations of oxidation-reduction enzymes were measured in the myocardium. Pathological changes in myocardial cells, disturbances of the microcirculation, and mitochondrial destruction in endothelial cells of the capillaries increased in severity with

increasing length of exposure. Ischemic foci formed in the myocardium. Changes were reversible after exposure ceased.

McKillop, I.G., D.S. Shepherd, P. Haynes, B.D. Pugh, J.L. Dagnall, and G. Denny. 1994. The behaviour of rats at an electrified grid and infrasound generator tested as a barrier for use in the Channel Tunnel. *Appl. Animal Behav. Sci.* 40(2):167-178. CABA record 94:93714. (Ref. No. 107)

An electrified grid positioned in front of a preferred food source was 98 to 99% effective in deterring rats from reaching the food. When a rail over the grid to the food was vibrated infrasonically, only one of the 12 rats learned to use the rail to get to the food. However, infrasound did not prevent the rats from walking on the rail. The frequency and sound pressure level were not given in the abstract.

Nekhoroshev, A.S. 1985. Exposure to low-frequency narrow-band noise and reaction of the stria vascularis vessels. *Vestn. Otorinolaringol.* (6):17-19. (Russian) BIOSIS record 1986:176862. (Ref. No. 64)

Rats were exposed to noise of frequencies 4, 31.5, or 53 Hz at 110 dB for 0.5 h, 3 h, or 3 h/day for 40 days. Infrasound exposure caused graver changes than exposure to sound at 31.5 or 53 Hz. Changes observed after exposure to this acoustic factor included reduced activity of alkaline phosphatase in the stria vascularis vessels and their impaired permeability. Impaired labyrinthine hemodynamics led to neurosensory hearing impairment.

Nekhoroshev, A.S., and V.V. Glinchikov. 1991. Morphofunctional changes in the myocardium under exposure to infrasound. *NVB. Noise Vib. Bull.* (reprinted from *Gig. Sanit.* No. 12:56-58, 1991). NIOSHTIC record 1997:182685. (Ref. No. 56)

Rats and guinea pigs exposed to infrasound (8 or 16 Hz) at 120 to 140 dB for 3 h/day for 1 to 40 days showed morphological and physiological changes in the myocardium:

- After a single 3-hour exposure at these levels, capillaries widened and arterial diameters decreased, which disturbed blood flow.
- Cardiomyocytes showed intracellular cytolysis.
- The activities of the redox (oxidation-reduction) enzymes succinate dehydrogenase and lactate dehydrogenase increased or decreased, changes being more pronounced at days 5 and 10.
- After 15 or 25 days of exposure,
 - granular dystrophy disappeared,
 - sarcoplasm became edematous and structures disappeared in the sarcoplasmic reticulum,
 - the Z-band region showed myofibrillar fragmentation,
 - redox enzymes were markedly reduced, and
 - DNA and RNA changes were evident.
- Changes were still evident at 40 days, but signs of cellular regeneration were observed and myofibrils reappeared.

Nekhoroshev, A.S., and V.V. Glinchikov. 1992a. Morphological research on the liver structures of experimental animals under the action of infrasound. *Aviakosm. Ekol. Med.* 26(3):56-59. (Russian) MEDLINE record 93214647. (Ref. No. 60)

Morphological and histochemical changes were studied in the hepatocytes of rats and guinea pigs exposed to infrasound (2, 4, 8, or 16 Hz) at 90, 100, 110, 120, 130, or 140 dB for 3 h/day for 5 to 40 days. Hepatocytes showed increased functional activity, but exposures for 25 and 40 days induced irreversible changes. Changes were more pronounced at 8 and 16 Hz than at 2 and 4 Hz. Exposures impaired cell organoids and nuclear chromatin. Single exposures did not induce any changes in the hepatocytes and small blood vessels.

Nekhoroshev, A.S., and V.V.Glinchikov. 1992b. Effect of infrasound on change in the auditory cortex. *Gig. Sanit.* (7-8):62-64. (Russian) BIOSIS record 1993:307064 (no abstract). [Reference attached] (Ref. No. 62)

Rats and guinea pigs (3 per sex per dose level) exposed to 8 Hz at 120 and 140 dB for 3 hours or 3 h/day for 5, 10, 15, 25, or 40 days showed changes in the heart, neurons, and auditory cortex increasing in severity with increasing length of exposure. The presence of hemorrhagic changes was attributed mostly to the mechanical action rather than to the acoustic action of infrasound. Changes in the brain may be more important than in the ears.

Shutenko, O.I., R.D. Gabovich, E.A. Krechkovskii, V.A. Murashko, and L.A. Stechenko. 1979. Effect of infrasound of varying intensity on the body of experimental animals. *Gig. Sanit.* (3):19-25. (Russian) MEDLINE record 79128740 (no abstract). [Reference attached] (Ref. No. 108)

Rats (30/group) were exposed 2 h/day for 4 months to 8 Hz at 90 dB (group 2), 115 dB (group 3), and 135 dB (group 4). The experiment was conducted under the same conditions as that used by Gabovich et al. (1979a) except that the latter used 20 rats per group. Eight of the 25 series of measurements reported here were also reported by Gabovich et al. (1979a) and are not repeated in this annotation. Findings among the additional parameters included the following, which were usually significant in groups 3 and 4:

- An increase in glycolytic activity in the brain
- Increases in cholinesterase and acetylcholinesterase activities in the brain and of acetylcholinesterase in the blood (not significant in group 3)
- Decreases of α -ketoglutarate and succinate dehydrogenase in hepatocyte mitochondria
- Increase in the degree of basophilic degranulation
- Decrease in working capacity
- An increase in gas exchange (not significant in group 4)

Shvaiko, I.I., I.P. Koairin, I.A. Mikhaliuk, and I.N. Motuzkov. 1984. Effect of infrasound on the metabolism of trace elements in the body. *Gig. Sanit.* (9): 91-92. (Russian) MEDLINE record 85102859 (no abstract). [Reference attached] (Ref. No. 109)

Rats exposed to 8 Hz for 4 months at 90, 115, or 135 dB exhibited statistically significant changes in copper, molybdenum, iron, and/or manganese concentrations in liver, spleen, brain, skeletal muscle, and/or femur compared to concentrations in the tissues of controls. Practically all tissues showed significant changes in all the elements for exposures at 135 dB. Changes included both elevations and depressions in concentrations. The trends were consistent with increasing sound pressure except for some tissue copper values.

Svidovyi, V.I., and O.I. Kuklina. 1985. State of the hemolymph circulatory bed of the conjunctiva as affected by infrasound. *Gig. Tr. Prof. Zabol.* (6):51-52. (Russian) MEDLINE record 85286518 (no abstract). [Reference attached] (Ref. No. [63](#))

Male rats (10/group) exposed to infrasound (8 Hz) at 100 and 140 dB for 3 h/day for 5, 10, 15, or 25 days showed constriction of all parts of the conjunctival vascular bed within 5 days. The decrease in the lumen of the capillaries was accompanied by swelling of the cytoplasm and the nuclei of the endotheliocytes. The capillaries, precapillaries, and arterioles became crimped. Morphological changes were reported in the vessels after exposure for 10, 15, and 25 days. After 25 days, increased permeability of the blood vessels led to swelling of tissues and surrounding capillaries and to perivascular leukocyte infiltration. Significant aggregates of formed elements of the blood were observed in the large vessels.

Svidovyi, V.I., V.N. Kolmakov, and G.V. Kuznetsova. 1985. Changes in the aminotransferase activity and erythrocyte membrane permeability in exposure to infrasound and low-frequency noise. *Gig. Sanit.* (10):73-74. (Russian) MEDLINE record 86109558 (no abstract). [Reference attached] (Ref. No. [110](#))

In studies of male rats (10/group) exposed to low-frequency noise or infrasound for 3 h/day for 5, 10, 15, or 25 days, changes in erythrocyte membrane permeability and enzyme concentrations depended primarily on the frequency and less on the intensity. The most sensitive index of injury was the increase in alanine aminotransferase activity in the serum. The increase in erythrocyte membrane permeability coincided with the increase of alanine aminotransferase, but the latter persisted longer. The alanine aminotransferase activity of liver tissue was lowered by the 15th day with 8 Hz at 140 dB and by the 15th to 25th day with 16 Hz at 130 dB. In the heart, exposure to 8 Hz at 140 dB lowered alanine aminotransferase activity by the 15th day yet increased the activity by the 25th day. When exposed to 8 Hz at 100 dB, alanine aminotransferase activity of the liver fell by the 15th day and became normalized by the 25th day.

Studies in Mice

Svidovyi, V.I., and V.V. Glinchikov. 1987. Action of infrasound on the lung structure. *NVB. Noise Vib. Bull.* 153-154 [translated from *Gig. Tr. Prof. Zabol.* (1):34-37, 1987]. NIOSHTIC record 1997:139492. (Ref. No. [65](#))

Histopathological and histomorphological changes were determined in the lungs of male albino mice exposed to infrasound (2, 4, 8, or 16 Hz) at 90 to 120 dB for 3 h/day for up to 40 days. Sectioned lungs were examined from selected mice sacrificed daily (numbers not given in the abstract). The following pathologies were reported after prolonged exposures:

- Exposure to 8 Hz at 120 dB caused filling of acini with erythrocytes and thickening of interalveolar septa.
- Exposure to 8 and 16 Hz at 140 dB ruptured blood vessel walls, partially destroyed acini, and induced hypertrophy of type-II cells. Type-II pneumocytes were activated in alveoli that were comparatively undamaged.

Studies in Guinea Pigs

Anichin, V.F., and A.S. Nekhoroshev. 1985. Response of the vessels of the guinea pig middle ear system to infrasonic exposure. *Gig. Tr. Prof. Zabol.* (9):43-44. (Russian) BIOSIS record 1986:180780 (no abstract). [Reference attached] (Ref. No. 66)

Guinea pigs (6 males/group) were exposed to infrasound (4 Hz) at 110 dB once for 0.5 hour or 3 hours or for 3 h/day for 40 days. After a single exposure, the vascular network of the tympanic membranes became more prominent than in the controls. The alkaline phosphatase activity increased chiefly in the endothelial and adventitious cells and also in the vessel walls of those guinea pigs exposed for 40 days.

Nekhoroshev, A.S., and V.V. Glinchikov. 1990. Mechanism of the effect of infrasound on labyrinthine receptors. *Kosm. Biol. Aviakosm. Med.* 24(6):39-42. (Russian) MEDLINE record 91155304. (Ref. No. 67)

Guinea pigs exposed to infrasound (8 or 16 Hz) at 90 to 120 dB for 3 h/day for 5, 10, 15, or 25 days showed morphological changes in receptor cells of all three semicircular canals and in hair cells of the spiral organ. Changes in the endoplasmic reticulum and mitochondria included swelling and shortening of the cristae. Recovery occurred after cessation of exposure.

Studies in Rabbits

Safonov, M.Yu. 1978. Histoenzymatic characteristics of the myocardium exposed to infrasound. *Gig. Tr. Prof. Zabol.* (12):52-55. (Russian) MEDLINE record 79066007 (no abstract). [Reference attached] (Ref. No. 68)

The activities of cytochrome oxidase and succinate dehydrogenase were measured in mitochondria of the myocardiocytes of rabbits exposed to infrasound (10 Hz) at 100 to 110 dB for 6 h/day for 24 days. Early rapid elevations of enzyme activities occurred in some regions compared to controls followed by depressed activities in all regions studied after about 6 days. Pathological changes caused by disturbances of the energy supply for the contractile activity of the heart were most expressed in regions with a high concentration of contractile function.

4.1.4 Synergistic/Antagonistic Effects

Some studies reported synergistic or antagonistic actions of infrasound and are described in annotations in other subsections. Two English references and 3 abstracts are available. See annotations in subsection 4.1.2 for Spyraakis et al. (39) (rats), Busnel and Lehmann (46,69) and Lehmann and Busnel (47) (mice). See annotations in subsection 4.1.3. for Dadali et al. (58) (rats) and Gabovich et al. (61) (rats) and in subsection 4.5 for Batanov (70) and Grigor'ev et al. (71).

4.2 Reproductive and Developmental Effects

Nine citations covering reproductive and developmental effects, carcinogenicity, genotoxicity, immunotoxicity, and other studies were considered for this report. English abstracts are available for 3 of these studies.

Only one study reported reproductive or developmental effects. Dadali et al. (58) [in subsection 4.1.3 (rats)] indicated that infrasound exposure caused dystrophic changes in the testicles of rats.

4.3 Carcinogenicity

None of the identified human or animal studies were relevant to potential carcinogenicity or anticarcinogenicity.

4.4 Genotoxicity

Svidovyi, V.I., and L.V. Kitaeva. 1998. Evaluation of cytogenetic activity in medullary cells exposed to infrasound. *Experimental data. Med. Tr. Promysh. Ekol. No. 5:42-44.* (Russian). MEDLINE record 1998327439 (no abstract). TOXLINE record 1998:142935 (no abstract). (Ref. No. [111](#))

According to the indexing of the MEDLINE and TOXLINE records, endpoints studied included aneuploidy, chromosomal aberrations, mitotic index, and, possibly, sister chromatid exchange, in bone marrow cells of male rats.

4.5 Immunotoxicity

Batanov, G.V. 1995. Characteristics of etiology of immediate hypersensitivity in conditions of exposure to infrasound. *Radiats. Biol. Radioecol. 35(1):78-82.* (Russian) MEDLINE record 95235736. (Ref. No. [70](#))

Dosing guinea pigs with an antigen that induced anaphylactic shock killed 80 to 100% of the animals within 3 minutes. Guinea pigs that were exposed for 10 minutes to infrasound of 10 Hz at 155-160 dB immediately before exposure to the antigen showed reduced fatalities since only 50 to 60% of the guinea pigs died. The experiment used 230 guinea pigs.

Grigor'ev, Yu.G., G.V. Batanov, and V.S. Stepanov. 1983. Changes in immunobiological reactivity under the combined action of microwave, infrasonic, and gamma irradiation. *Radiobiologiya 23(3):406-409.* (Russian) MEDLINE record 83248063. (Ref. No. [71](#))

These experiments with rats and rabbits studied the combined effects of microwaves (9.3 g Hz and 0.1 GHz at 200 and 1530 $\mu\text{W}/\text{cm}^2$), infrasound (8 Hz, 115 dB), and gamma irradiation (5.5 Gy) on cell and humoral immunity and on autoimmune processes. Microwave treatment protected against the biological effects of gamma radiation whereas infrasound plus microwave treatment enhanced the effects.

See also Gabovich et al. ([61](#)) in section 4.1.3 (last statement in annotation).

4.6 Other Studies

This section includes an *in vitro* study and studies in which the duration of *in vivo* exposure was not clear.

Shcheglov, A.G., and E.M. Baranov. 1972. The effect of infrasound on the functional state of cells in the central nervous system and some internal organs. *Tr. Leningr. Sanit.-Gig. Med. Inst. 97:79-82.* (Russian) BIOSIS record 1973:226271 (no abstract). (Ref. No. [112](#))

According to the index terms, infrasound induced pathological changes in the brain, lungs, liver, and, probably, the ears (sense organs) of mice.

Svidovyi, V.I., and V.V. Glinchikov. 1991. Response of nervous system cells to infrasound. *Gig. Tr. Prof. Zabol.* (6):37-38. (Russian) BIOSIS record 1992:13828 (no abstract). (Ref. No. 113)

According to the indexing terms of the BIOSIS record, the endpoints of concern after rats were exposed to infrasound included brain cells, ischemia, and capillary resistance.

Svidovyi, V.I., and A.G. Shleikin. 1987. Effect of infrasound on tissue succinate dehydrogenase activity. *Gig. Tr. Prof. Zabol.* (5):50-52. (Russian) MEDLINE record 87277547 (no abstract). (Ref. No. 114)

According to the indexing terms of the MEDLINE record, succinate dehydrogenase activity was measured in the myocardium and brain tissues of rats.

Svidovyi, V.I., V.N. Kolmakov, V.A. Kuleba, and V.M. Timofeeva. 1987. Change in the permeability and total ATPase activity of erythrocytes and blood plasma superoxide dismutase activity on exposure to infrasound in vitro. *Gig. Sanit.* (5):78-79. (Russian) MEDLINE record 87277495 (no abstract). [Reference attached] (Ref. No. 72)

Rat whole blood samples stabilized with 1.34% sodium oxalate were exposed to infrasound (2, 4, 8, and 16 Hz) at 110, 120, 130, and 120 dB, respectively, for 3 hours. At 16 Hz and 120 dB, ATPase activity decreased while activity was increased by exposure to infrasound at 2 Hz. Superoxide dismutase (SOD) increases depended on the frequency. No SOD increases were observed at 2 Hz. [Partial data extraction from the Russian.]

5.0 Databases Used and Search Strategy

The biomedical databases MEDLINE, CANCERLIT, TOXLINE, AGRICOLA, NIOSHTIC, CABA, EMBASE, BIOTECHNO, ESBIODBASE, BIOSIS, and LIFESCI were searched simultaneously on the STN International system on August 28 and 29, 2001. The NTIS database was searched separately. The Google search engine was used to search the Internet in the period August 28 through September 16, 2001, for various concepts related to infrasound.

In the biomedical databases, the terms infrasound OR infrasonic? (where ? is a truncation symbol) found 711 records. Combination with the terms review? OR review/DT (where DT = document type) found 69 records. The abstract and indexing of the full database records of the reviews were examined for appropriate keywords.

After the reviews were subtracted, the remaining records were searched by combining the answer set with the following terms:

health OR hygien? OR biomedical? OR etiol? OR hypersensitiv? OR endolymphatic OR morpholog? or pneumomassage OR disease OR ischemi? OR ischaemi? OR risk? OR harm? OR danger? OR hazard? OR adverse OR safe? OR (biological OR physiological)(w)effect? OR impair? or hearing(w)loss?

The combination resulted in 281 hits, which were reduced to 220 after automated duplicate removal. The titles of the 220 records were examined (in alphabetical order by title to detect additional duplicates) and several were selected for printing in full. The breakdown of number of citations by database is shown below:

Source	Number of Citations	Number of Full Records Retrieved
MEDLINE	62	51
TOXLINE	54	24
NIOSH TIC	37	18
CABA	5	0
EMBASE	39	16
BIOSIS	20	9
LIFESCI	3	1

After previous answer sets were eliminated, the remaining records were combined with additional terms, which included laboratory animal species; terms for humans (man OR men OR human? OR volunteer? OR subject? OR pilot? OR driver? OR worker?); epidemiol?; massage?; and endpoints or target tissues (annoy? OR nystagmus OR myocardi? OR behavior? OR behaviour? OR psychol? OR physiol?). The resulting set of 260 records was reduced by automated duplicate removal to give 185 records whose titles were also examined to select records for printing in full. The breakdown of number of citations by database is shown below:

Source	Number of Citations	Number of Full Records Retrieved
MEDLINE	53	28
TOXLINE	15	8
AGRICOLA	3	2
NIOSH TIC	8	3
CABA	7	0
EMBASE	35	23
ESBIOBASE	3	0
BIOSIS	56	24
LIFESCI	5	1

Searches were also conducted in NTIS. The strategy eliminated records containing the terms seismic?, detect?, earthquake?, sensor?, nuclear, physics, and China (re: detection of underground explosions). Fourteen records were selected for printing in full after examination of the resulting 156 titles.

6.0 References for Sections 1.0, 2.0 and 3.0

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Acknowledgements

Support to the National Toxicology Program for the preparation of Infrasound—Brief Review of Toxicological Literature was provided by Integrated Laboratory Systems, Inc., through NIEHS Contract Number N01-ES-65402. Contributors included: Karen E. Haneke, M.S. (Principal Investigator); Bonnie L. Carson, M.S. (Co-Principal Investigator); Claudine A. Gregorio, M.A., and Elizabeth A. Maull, Ph.D.

Appendix: Abbreviations and Acronyms

ACGIH	American Conference of Governmental Industrial Hygienist
ACTH	adrenocorticotrophic hormone; in ref #41
ADP	adenosine diphosphate
AMP	adenosine monophosphate
AN	ambient noise; in ref #34.
AP	auditory evoked potential; in ref #52
ATP	adenosine triphosphate
ATPase	adenosine triphosphatase
bel	Unit of measure of sound level or intensity ratio. 1 bell corresponds to an intensity ratio of 10, 2 bels to 100, 3 bels to 1000, and so on.
BN	background noise in ref #34.
dB	decibels; unit of sound level equal to 1/10 of a bel
dba	decibels on A-weighted scale; in ref #30 and 85
ECG	electrocardiograph; in ref #33
ENG	electronystagmography; in ref #33
EP	endonuclear potential; in ref #51
FDA	Food and Drug Administration
GHz	GigaHertz (unit of frequency: 1,000,000,000 cycles per second)
GSR	galvanic skin response; in ref #33
Hz	Hertz; a unit of frequency, equal to one cycle per second
kHz	Kilo Hertz (unit of frequency, 1000 cycles per second)
m	meter
min	minutes
mm Hg	mm Mercury; measure of blood pressure
NTIS	National Technical Information Service
OKN	not found; in ref #33
OSHA	Occupational Safety and Health Administration
phon	Unit of subjective measure of sound intensity. 1 phon is equal to 1 dB only at 1000 Hz. At lower frequencies the value in phons is greater than the value in decibels.
redox	oxidation-reduction
SPL	sound pressure levels
SOD	superoxide dismutase

TTS temporary threshold shifts in ref #27
UHF ultrahigh-frequency (electromagnetic fields); in ref #61
WHO World Health Organization