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Guidelines for Assessing the Toxic Hazard of Spacecraft Chemicals and Test Materials

Human Health and Performance Directorate

Biomedical Research and Environmental Sciences Control Board (BRESCB)

Revision B

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National Aeronautics and Space Administration
Lyndon B. Johnson Space Center
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NASA APPROVAL SHEET

Guidelines for Assessing the Toxic Hazard of Spacecraft Chemicals and Test Materials

Human Health and Performance Directorate

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CHANGE HISTORY

Status	Revision No.	Change No.	Description	Release Date
Baseline	-		Approved at HHPCB	09/1997
Revision	A		Approved at HHPCB, per HHPD-BRES_CB-14-002 Prepared By: Hector Garcia Toxicologist Environmental Sciences Branch Change Summary: Revised / updated to reflect changes to NASA programs. Update to process descriptions throughout document. Revision of Table 1.	04/30/2014
Revision	B		Approved at HHPCB, per SA-C20032 Prepared By: Valerie Ryder Toxicologist Environmental Sciences Branch Change Summary: Revised to include generalized updates to group names, NASA Programs, and references to current tools. Include information documented between updates in memorandum of understanding for physical hazards (particles and asphyxiant gases) and aldehyde fixatives. Include GHS classification to THL defaults.	07/01/2025

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1.0 INTRODUCTION

1.1 PURPOSE AND SCOPE OF THIS DOCUMENT

This document describes the criteria and procedural guidelines used by the NASA / Johnson Space Center (JSC) Toxicology Group to perform toxicological evaluations. JSC Toxicology is responsible for conducting toxicological assessments and assigning toxic hazard levels (THLs) for essentially all chemicals and test materials to be used in or transported to the habitable areas of U.S. spacecraft, non-U.S. spacecraft inhabited by U.S. crew members or habitable areas of off-Earth habitats, vehicles, and spacesuits where U.S. crew members would be present, including chemicals carried by visiting spacecraft (visiting vehicles) to and from the International Space Station (ISS) or Exploration destinations. This document will focus on the assessment of chemically-induced toxicity hazards. It also briefly addresses the assessment of physical hazards associated with chemically inert substances. Other hazards, including biosafety, radiation, and flammability, are handled by other groups under different processes. The toxicological assessments, together with assessments on radioactive, biological, physical, and flammability hazards as well as impacts to environmental control systems, are incorporated into a mission-specific Hazardous Materials Summary Table (HMST).

1.2 PURPOSE OF TOXIC HAZARD ASSESSMENTS AND THE HAZARDOUS MATERIALS SUMMARY TABLE

Safety is of the highest priority to NASA. Thus, minimizing adverse effects on crew health from exposure to hazardous materials in spacecraft is a major NASA objective. In supporting NASA's safety objective, JSC Toxicology assumes responsibility for compiling information on, assessing the potential adverse effects of, and assigning THLs to all in-flight chemicals to which the crew might be exposed. Data for these substances must be submitted per JSC 27472 *Requirements for Submission of Data Needed for Toxicological Assessment of Chemicals to be Flown on Crewed Spacecraft*. The assigned hazard levels are used by payload, system, or government furnished equipment (GFE) developers as criteria in the design of flight hardware to assure adequate containment. For experiments, systems, and other payloads, including GFE, flying in the pressurized volume of NASA spacecraft (or other vehicles docking to spacecraft that NASA crew may occupy), it is the responsibility of the governing NASA Safety Panel to certify that the design of equipment provides adequate containment for the assigned hazard levels of the materials it contains. The assigned THLs, along with other hazard levels, are compiled in a Hazardous Materials Summary Table (HMST). These files are created and maintained in the electronic HMST database (eHMST). HMST record sets are utilized by designated Safety Panels when reviewing payload and systems chemicals and materials, by crew members aboard the ISS and other habitable vehicles and habitats, and by ground-support professionals in the event of on-orbit chemical/materials leaks during missions.

1.3 COMPILATION AND DISTRIBUTION OF TOXICOLOGICAL HAZARD INFORMATION

The assessment process begins with payload investigators, system/GFE managers, or coordinators submitting information and relevant data on payload chemicals as described in JSC 27472. JSC toxicologists enter relevant data, together with the toxicological assessments and assigned THLs into eHMST. Once all subject matter expert (SME) assessments are complete, including toxicology, the HMST is available to authorized payload, system, or GFE organizations to verify the accuracy of the information on the chemicals or biological materials that they intend to fly. Providers link the eHMST record to the relevant hazard record for use during Safety reviews. Mission-specific HMSTs are available to flight surgeons, biomedical flight controllers (BMEs) and other mission support personnel and are loaded onto onboard spacecraft computers and available in the Mission Control Center to provide real-time toxicological support.

2.0 APPLICABLE DOCUMENTS

The following documents include specifications, standards, guidelines, handbooks, and other special publications which document processes that utilize the THLs defined here.

Document Number	Document Title
JSC 27472	Requirements for Submission of Data Needed for Toxicological Assessment of Chemicals to be Flown on Crewed Spacecraft
JSC 20584	Spacecraft Maximum Allowable Concentrations for Airborne Contaminants
SSP 51721	ISS Safety Requirements Document
MPCV 70038	Orion Multi-Purpose Crew Vehicle (MPCV) Program Hazard Analysis Requirements
MPCV 70024	Orion Multi-Purpose Crew Vehicle (MPCV) Program: Human Systems Integration Requirements (HSIR)
GP 10024	Gateway Program Hazard Analysis Requirements

GP 10017	Gateway Human System Requirements (HSR)
HLS-RQMT-002	Human Landing System (HLS) Provider System Requirements Document (PRSRD) – Initial Phase
HLS-RQMT-006	HLS Integrated Lander Requirements Document – Sustained Phase
HLS-RQMT-007	HLS Human-Class Delivery Lander (HDL) Requirements Document – Sustained Phase
HLS-RQMT-008	HLS Human-Class Delivery Lander (HDL) Provider System Requirements Document (SRD) (SpaceX)
HLS-RQMT-009	HLS Provider Integrated Lander System Requirement Document – Sustained Phase (SpaceX)
HLS-RQMT-108	HLS Human-Class Delivery Lander (HDL) Provider System Requirements document (SRD) (Blue Origin)
HLS-RQMT-109	HLS Provider Integrated Lander SRD – Sustained Phase (Blue Origin)
M2M-30047	Moon to Mars (M2M) Cross Program Utilization Payload Safety Process

3.0 DEFINITION OF TOXIC HAZARD LEVELS (THLS)

The definitions and criteria for THLs are shown in Table 1. The THL of an escaped chemical depends on its physicochemical properties (e.g. gas, liquid, solid, particle size, acidity, alkalinity, and corrosiveness), its quantity, its adverse effects (e.g. irritancy, carcinogenicity, systemic toxicity), and the ease with which the chemical is removed from the environment. The removal rate depends on a combination of the characteristics of the spacecraft's life support system and the chemical's physicochemical properties.

TABLE 1 GENERAL DESCRIPTION OF TOXICOLOGICAL HAZARD LEVELS

Toxicity Hazard Level (Hazard Classification) (Color Code) Physical State	Irritancy	Systemic Effects	Containability and Mitigation
0 (Negligible/Marginal) (Green) Gas, solid, or liquid	Slight irritation that lasts <30 minutes and will not require therapy.	None	May or may not be containable. No PPE required but may be donned by crew at their discretion.
1 (Critical) (Blue) Gas, solid, or liquid	Slight to moderate irritation that lasts >30 min and will require therapy	Minimal effects, no potential for lasting internal tissue damage.	May or may not be containable. Crew should don PPE according to applicable procedures/flight rules.
2 (Catastrophic) (Yellow) Either a solid or nonvolatile liquid	Moderate to severe irritation that has the potential for long-term performance decrement and will require therapy. Eye Hazards: May cause permanent damage.	Minimal effects, no potential for lasting internal tissue damage.	Can be disposed of and contained by a cleanup procedure. Crew should don PPE according to applicable procedures/flight rules.
3 (Catastrophic) (Orange) Either a solid or low-volatility liquid	Negligible to severe irritation may accompany systemic toxicity; however, irritancy alone does not constitute a level 3 hazard.	Appreciable effects on coordination, perception, memory, etc., or has the potential for long-term serious injury (e.g. cancer), or	Can be disposed of and contained by a cleanup procedure. Crew should don PPE according to applicable procedures/flight rules.

		may result in internal tissue damage.	
4 (Catastrophic) (Red) Gas, volatile liquid, or fumes that are **not containable**	Moderate to severe irritancy that has the potential for long-term crew performance decrement (for eye-only hazards, there may be a risk of permanent eye damage). Note: Will require therapy if crew is exposed.	Appreciable effects on coordination, perception, memory, etc., or the potential for long-term serious injury (e.g. cancer) or may result in internal tissue damage.	Crew **cannot** contain the spill. The ECLSS may be used to decontaminate. Crew should don PPE according to applicable procedures/flight rules.

4.0 GENERAL GUIDELINES BY WHICH TOXICOLOGICAL HAZARDS AND TOXIC HAZARD LEVELS ARE ASSESSED

Chemicals and test materials to be used in experiments or other activities aboard the spacecraft can be gases, gels, liquids, or solids, which include fine particulates. They can be pure chemicals, solutions, complex mixtures, metallic alloys, etc. During processing, some materials used in in-flight experiments may undergo changes in phase (e.g. solid to liquid or gas or to vapor or fume), undergo chemical reactions to produce new chemicals (e.g. combustion), or undergo changes in concentration (e.g. dilution). Materials can be classified as organic, inorganic, polymeric, biological, radioactive, acidic, basic, neutral, oxidants, hypertonic or hypotonic. These chemical, physical and/or biological properties, together with their intrinsic toxicity, flammability, and biohazard potential, determine the hazard response level of the materials. Because the range of potential materials and quantities is so broad, no one set of standard procedures can describe how JSC Toxicology assesses every possible material. Some general guidelines described below are applicable for assessing most chemicals. Other procedures applicable to individual classes of chemicals or materials are described in Section 4.

4.1 IDENTIFYING IN-FLIGHT CHEMICALS

JSC Toxicology assesses the potential toxic hazards of chemicals and test materials used or contained in in-flight payload experiments, equipment, and hardware (e.g. GFE, crew escape equipment, etc.) during all phases of flight (launch, stowage, operations, and return). The chemical information is provided by mission managers, payload integration managers, payload organizations or investigators and others. Payload, system, and GFE hardware customers are required to submit complete and accurate information on chemical identities, composition, physical states, concentrations, amount, test conditions and other relevant information, as specified in JSC 27472, as part of their safety data packages prepared for safety reviews.

4.2 ASSESSING THE TOXIC HAZARDS OF RELEASED CHEMICALS

The THL of a payload chemical is defined in terms of the risk to crew health from an accidental spill or leak of that chemical. Except in cases where a single failure may lead to the simultaneous release of multiple containers (see below), it assumes the full amount of a single container and depends on the intrinsic toxicity and physical properties of the chemical. That is, the default assumption is that the full amount is released, and crew contact occurs. An exception to this rule is made for chemicals entrapped in a matrix (cloth wipe or agar gel, as examples) that would prevent their escape or rapid release. When confirmed by Safety, such entrapment is considered by the toxicologist in setting the THL. A payload, system, or GFE hardware customer may propose multiple levels of containment for a highly toxic chemical to minimize its chance of release. While this would not alter the THL of the chemical, it would reduce the risk to crew health. Assessment of the adequacy of containment is the purview of the NASA-designated Safety Panel.

Safety can review and determine that the conservative default of full release of a single container is non-credible. In that case, the designated Safety Panel will direct JSC Toxicology to assume less than full release (to be specifically defined). The alternate assessment conditions and direction from the Safety Chair or designee will be included in the assessment and as attachment(s) in the eHMST tool.

4.3 ANALYZING THE HAZARD OF CHEMICAL MIXTURES

The THL of a mixture of chemicals is determined from the toxicity of the entire mixture or, if that is unknown, the most toxic component in that mixture.

4.4 ASSESSING CHEMICALS THAT UNDERGO PHASE OR COMPOSITION CHANGES DURING PROCESSING OR CONCENTRATION CHANGES AFTER MIXING

If chemicals or mixtures pose different toxicological hazards to crew members before, during, or after processing or operations, all of these stages are assessed. For example, if a liquid is to be mixed with another liquid, then the resultant mixture is also assessed.

4.5 CALCULATING POTENTIAL ATMOSPHERIC CONCENTRATIONS OF CHEMICALS ON THE SPACECRAFT

When fine dusts, metallic fumes, gases, or vapors from volatile liquids escape in the spacecraft, these substances become airborne and could pose a toxicity concern. The concentration of the released chemical is determined by dividing the mass by Program-approved standard volumes. The THL of these chemicals will depend on the resultant cabin concentrations, which can be estimated by dividing the amount of escaped chemical by the relevant spacecraft habitable volume or the relevant spacecraft module volume. Assessment of volume-dependent chemicals on Exploration vehicles will be case-by-case based on planned mission architecture for any given flight. The vehicle or cabin concentrations will be compared to the saturated vapor

concentration when appropriate and the lesser of the two values will be chosen. This prevents assessing for a concentration above which is possible.

There may be cases for which crewed spacecraft or crewed space habitats will not dock/berth with the ISS and therefore habitable volume information will not be found in SSP 50623. Information concerning the relevant spacecraft volume of dilution will, in these cases, be obtained from the most recent official design specification documents of record for that vehicle or habitat.

4.6 ESTIMATING THE RATE OF REMOVAL OF AN ESCAPED CHEMICAL

The time needed for the environmental control and life support system (ECLSS) to remove specific types of toxicants from the atmosphere depends upon many factors. These include the amount of the chemical that has escaped, its chemical and physical properties, the total volume of air to be scrubbed, the rate of cabin airflow through the various air scrubbers, the ability of the air scrubber's absorbent materials to retain specific contaminants, the mesh sizes of the air filters used to retain particulates, the relative humidity of the atmosphere, and the condensing and solution of vapors into water formed by the condensing heat exchanger (dehumidifier). Sometimes it is only possible to make a rough estimate of removal times or contaminant concentrations during and after scrubbing. ECLSS experts provide impacts of release of chemicals in the HMST assessment process. They will also be consulted as required to inform the toxicological assessment of large releases of chemicals that rely on ECLSS for clean-up (cannot be cleaned up by crew).

4.7 IDENTIFYING POTENTIAL EXPOSURE ROUTES AND TARGET ORGANS

Of the various ways in which U.S. crew members or other space vehicle occupants could be exposed to an escaped chemical, ingestion (i.e. oral route) is considered least likely because they would not open their mouths to allow the chemical to enter and then swallow it. Therefore, this route of exposure is generally not assessed except in special cases. Most chemicals spilled on the skin can be readily removed; skin absorption is usually very slow. This route of exposure typically poses only minimal risk (irritancy) except in the case of highly corrosive materials, such as concentrated acids and bases and those few compounds, such as phenol, which are absorbed through the skin at a rate sufficient to cause systemic toxicity. Non-volatile liquids are routinely assessed primarily for their eye irritancy. Any liquid reaching the eye would potentially remain there for several minutes before mitigation steps could be taken (e.g. time to destow and utilize an eyewash). Surface tension without gravity or in micro-gravity fields can allow relatively large volumes of liquid to contact the eye. Since no more than about 0.5 ml of liquid could contact the eye due to its small surface area, small or large volumes of liquid would pose similar eye hazard levels. Volatile liquids are assessed for contact irritancy (eye/skin), and their vapors are assessed for irritancy to the eyes and respiratory tract and for systemic toxicity. The major concerns posed by metallic fumes, dusts, and gases are respiratory tract irritancy and systemic toxicity. Very high concentrations of dusts can pose a risk of

asphyxiation. Chemically inert particles are assessed per memorandum TOX-VR-2023-01, Rev G (or most current revision). Microorganisms, animals, plants, as well as products from each of these sources such as blood cells, etc., are assessed by the Biosafety Review Board for their infectious potential, but some biological materials, are also assigned a toxicity hazard level; an example is vomitus due to its low pH.

An allergic reaction to a chemical often depends on an individual's immunological responses to such a chemical; the interaction between host and the chemical, and the magnitude of allergic response are very difficult to predict or quantify. There are, however, several chemicals that are known to cause skin sensitization when exposure reaches a certain threshold, which can in turn cause predictable but delayed responses to these chemicals. For such chemicals, their individual sensitization thresholds will be considered during assessment. For chemicals that are not known to cause sensitization, unless the chemical is a known allergen to the general population, their allergenic potential is generally not considered in our toxicological assessment.

4.8 USING SPACECRAFT MAXIMUM ALLOWABLE CONCENTRATIONS (SMACS) AND OTHER PUBLISHED LIMITS IN DETERMINING THLS

NASA has established 1-hour, 24-hour, 7-day, 30-day and 180-day spacecraft maximum allowable concentrations (SMACs) for approximately 60 airborne chemicals. 1000-day SMACs are established for a subset of these chemicals. Generally, these exposure limits allow minor discomfort during 1-h or 24-h exposures and no discomfort or risk of toxicity for longer exposures. Short-term SMACs are generally most applicable for evaluation of unexpected, accidental chemical release. In addition, NASA has many documented interim SMACs. These interim limits undergo internal rigor and review but are not sent for external peer review. Impacts of altered atmospheres (i.e., reduced pressure with increased oxygen) will be considered per JSC 20584 *Spacecraft Maximum Allowable Concentrations for Airborne Contaminants*.

If SMACs are not established, emergency limits (protective action criteria) or immediately dangerous to life and health limits may be referenced. These are intended to protect the general population, including sensitive subgroups, and are therefore likely conservative for spaceflight application but do provide a reasonable basis for assessment.

In the absence of both SMACs and emergency limits, occupational limits, including threshold limit values (TLVs), permissible exposure limits (PELs) and recommended exposure limits (RELs), may be referenced. These limits are established to protect nearly all industrial workers exposed up to 8 hours per day, 40 hours per week for their entire working lifetime, generally assumed to be 40 years.

NASA's THLs (see Table 1) are based on the severity of eye irritancy, systemic toxicity, potential for permanent tissue injury, and the ability of the crew and the spacecraft environmental control and life support system to decontaminate or remove that material.

Since SMACs, and THLs are based on different criteria and are meant to be used in very different circumstances, no precise, quantitative relationship exists between them nor are there SMAC (or other occupational limit) equivalents to the critical and catastrophic levels in the THL scale. However, there is usually a rough relationship among these three standards. For example, if the potential spacecraft concentration of an airborne chemical vapor is less than or equal to the SMAC, emergency or occupational limit, it is generally assessed as THL = 0 (marginal hazard). The toxic hazard rating of concentrations greater than the SMAC or an occupational limit will depend on the intrinsic toxicity and physicochemical properties of the chemical.

4.9 DETERMINING THE INTRINSIC TOXICITY

As discussed above, the physiochemical properties of chemicals and test materials are very diverse, and their toxicities can vary greatly. Toxicity is judged by available information from reference books, computerized toxicology databases or scientific literature, or assessments performed for past HMSTs. Safety Data Sheets (SDSs) and information on the biochemistry and toxicity of the proposed chemicals obtained from the payload providers or chemical manufacturers may also be used. Information on structurally-related compounds may be used to infer the toxic properties of the compound of interest. In some cases, little or no data are available for particular chemicals, and assessment requires a considerable amount of professional judgment and conservatism.

4.10 ASSIGNING TOXIC HAZARD LEVELS

After all of the above relevant steps are completed, a JSC toxicologist assigns a THL to the chemical or test material according to the definitions specified in Table 1 and following the guidelines contained in this document. If the THL cannot be readily assigned using these definitions, it is rated on the basis of the best match between the table definitions and the toxicological properties of the material. THLs are assessed on a mission-specific basis.

If chemicals were assigned a THL for a previous mission, the same rating is generally applied. Occasionally, however, new toxicologically-relevant data become available or vehicle-specific parameters change that may lead to a revision of previous hazard assessments and ratings. If the chemicals being assessed have never been reviewed by JSC Toxicology or there is a need to change a previous THL, then a second toxicologist will review the new assessment. If the second Toxicologist does not concur with the new/revised assessment, then all available toxicologists will review the assessment and related data. A THL will then be assigned based on the outcome of the quorum review. A quorum review is also required for all potential THL 4 hazard ratings except where hazard thresholds have been specifically defined in JSC Toxicology memorandum.

5.0 PROCEDURAL GUIDELINES FOR ASSESSING THE TOXICOLOGICAL HAZARD LEVELS OF CHEMICALS

5.1 METALS AND METALLIC COMPOUNDS USED IN METALLURGICAL (FURNACE) EXPERIMENTS

Metals and metallic compounds can vaporize when heated to high temperatures and condense into fumes and fine dusts upon cooling. The toxic hazard level depends on the amount and toxicity of the metallic vapors or fumes produced during processing. If the investigators can provide the evaporation rates of the metals in an alloy or estimated amounts of fumes that could be generated from the alloy during processing, or if they have data on sample weight loss due to heating of the naked alloy sample, JSC toxicologists will use this data for toxicity hazard assessment. If calculated or experimental data from the payload developer are unavailable, JSC toxicologists will use the simplified Langmuir's Law for estimation of the evaporation rate, Q (mg/cm2/second) of the metals in the alloy.

$$Q = 43.7\ (M/T)^{0.5}P$$

M is the atomic weight (a.m.u.) of a given metal, T is the planned maximum processing temperature (K), and P is the vapor pressure (mbar) of the metal at temperature T. P can be found from the literature or from a vapor pressure vs. temperature curve (see Appendix B. The amount of fumes of a metal that could be generated during processing, A (mg), can be estimated as follows:

$$A = Q\ S\ t$$

where S is the surface area (cm^2) of the alloy occupied by that metal and t (seconds) is the processing time at the maximum (holding) temperature. For example, if the alloy contains 20% of metal X and has a surface area of 5 cm^2, the surface occupied by metal X is considered to be 1 cm^2. The amount of metal vapor generated during the heating and cooling phases is relatively small compared to that generated during the holding temperature, unless the holding time (at maximum temperature) is short compared to the heating and cooling time. If the holding time is relatively short, the assessment will be evaluated case by case. If experimental data are not available, the investigators are encouraged to estimate the metallic fume production of their samples using the above formula or another more appropriate equation.

Depending on the circumstances of an experiment, the temperature used in the formula above could be either the nominal maximum planned temperature or the maximum "run-away" temperature (i.e., caused by experimental or control failure). JSC Toxicology generally uses the maximum run-away temperature projected by the payload developer for calculations unless directed by the appropriate Safety Panel to use an alternative working temperature (e.g. maximum nominal planned temperature) for a given experiment. If a run-away temperature is not available, JSC Toxicology will use the maximum nominal planned temperature for calculation. Because the metal surface will decrease with heating time, and vaporization will

cease after the vapor reaches saturation inside the confined space of the sample container, the value of the empirical calculation is generally greater than the amount of fume actually generated during processing.

From the calculated amounts of metallic fumes that could be generated from each metal in an alloy, the potential spacecraft cabin atmospheric concentrations of metallic fumes can be estimated in the event of their escape into the cabin as follows:

$$C = \frac{A}{V}$$

where A (mg) is the total mass of fumes, V (m^3) is the spacecraft cabin volume and C (mg/m^3) is the concentration (see section 3.5).

The time-weighted average concentrations of vapors, fumes, or dusts (including rates of release and removal by scrubbing from the atmosphere by ECLSS) can often be estimated mathematically. When appropriate, such calculations should be used on a case-by-case basis in assessing the THL of this class of airborne contaminants.

A metal fume or dust with a calculated concentration of less than or equal to one times the applicable TLV will generally be rated a THL of zero (0). A calculated concentration of non-irritating and low toxicity fume or dust of greater than one times the applicable TLV but less than ten times the applicable TLV will generally be rated a THL of one (1, critical hazard) or less. An irritating or toxic fume or dust concentration calculated to be equal to or greater than ten times the applicable TLV will generally be rated a THL of four (4, catastrophic hazard). A calculated fume or dust concentration that could pose a catastrophic hazard will be critically assessed by at least two JSC toxicologists.

5.2 PARTICULATES OTHER THAN METAL FUMES OR DUSTS

5.2.1 INERT, INSOLUBLE, NUISANCE PARTICLES

Large amounts of inert, essentially insoluble, nuisance particles pose a hazard to crew members if they are inhaled and cause physical blockage of the respiratory tract or if they contact the eye surface. If the quantity of released particles of the size ranges described below reach a level in the atmosphere that could cause choking/asphyxiation, this will be classified as a physical, rather than a toxicological hazard to the crew. Hazard assignments of non-toxic, insoluble, inert dust will be based on JSC Toxicology memorandum *TOX-VR-2023-01, Rev G* (or most current revision) which assigns physical hazard classifications to various concentrations depending on particle size. This physical hazard assessment is performed separately from the THL assessment, which separately evaluates chemical toxicity of the particles.

“Large” particles: Inert, insoluble, nuisance particles of mean aerodynamic diameter >10 µm cannot be inhaled deeply into the lower respiratory tract (lungs), but large amounts could cause

acute asphyxia (suffocation within a few minutes) due to mechanical blockage of the upper respiratory tract. Such particles will be considered a choking hazard at estimated initial concentrations of ≥ 50 g/m^3, assuming uniform distribution in the pressurized atmosphere of the vehicle or module where the particle release has occurred.

"Small" particles: Inert, insoluble, nuisance particles of mean aerodynamic diameter ≤10 µm can be inhaled deep into the lungs and cause a slow asphyxiation (suffocation within many minutes to hours) by obstructing the deep lung and interfering with oxygen exchange. For such respirable particles, an estimated initial concentration of ≥ 13 g/m^3 in the vehicle or module where the release has occurred will be classified as an asphyxiation hazard. This estimate is based on a particle density of 1.5 g/cc, 50% deposition in the lungs, and assumes that the exposed individual has a minute volume of 10 liters/min during an exposure duration of about 360 minutes, divided by a safety factor of 2. The concentration limit will therefore differ for different minute volumes or particle densities.

5.2.2 REACTIVE, TOXIC, OR SOLUBLE PARTICLES

Particles that are chemically reactive, toxic, and/or appreciably soluble in water will be assessed for toxicity on a case-by-case basis. The inhalation toxicity of these particles will depend mainly on their respirability, chemical reactivity, intrinsic toxicity, and irritancy. Generally, the smaller the aerodynamic diameter of the particles, the greater their ability to cause injury deep into the lung. Larger particles would exert their toxic effects on the upper respiratory tract. The ocular toxicity of these particles will similarly depend on size, chemical reactivity, and irritancy.

5.2.3 NANOPARTICLES

Nanoparticles are particles ranging in size from 1 to 100 nanometers. They may be used in experimental payloads or generated by activities such as 3-D printing processes. For these, hazard control measures to limit exposures should be implemented. The Occupational Health and Safety Administration (OSHA) recommends that work with nanomaterials occur in ventilated enclosures (e.g., glove box, laboratory hood, or process chamber) equipped with high-efficiency particulate air (HEPA) filters.

5.3 GASES

Gases stored in pressurized vessels are sometimes used in payload experiments. The potential toxicological hazard of a released gas is assessed based on the amount of that gas in the cylinder, the resultant concentration in the spacecraft atmosphere and its intrinsic toxicity or flammability. Removal rates by the Atmospheric Revitalization System (ARS) may be factored into the toxicological assessment. Gases can also present an asphyxiation hazard if their release results in a substantial decrease in oxygen concentration in the area. Assessments should take into account the volume of the potential hypoxic area and the rate of airflow in the vicinity of such a potential release. The impacts of oxygen reduction may be amplified by the slightly hypoxic starting conditions of exploration atmospheres. Rapid release of simple gas asphyxiants

that are not inherently toxic at concentrations below which may displace oxygen present a physical hazard analogous to inert particles and are assessed per JSC Toxicology memo *TOX-VR-2023-04 (or most current revision)*.

Oxygen toxicity may potentially occur if a large amount of oxygen is rapidly released in the spacecraft atmosphere. Potential toxicological hazard of exposure to hypertoxic environments is assessed based on the oxygen partial pressure requirements described in the Aeromedical Flight Rule BR13-54 document. Table BR13-54-II in the flight rule document provides guidance on the allowable maximum crew exposure duration to different elevated oxygen ranges in the ISS 14.7 psia environment. As exploration atmospheres generally have lower atmospheric pressures than the ISS, the oxygen requirements to sustain adequate crew oxygenation are slightly elevated. As such, recommendation of crew exposure duration in exploration environments are based on adjusted oxygen thresholds that account for the lower atmospheric pressure.

Assessments are also performed on vapors that may be generated from volatile or semi-volatile liquids with vapor pressure ≥ 10Pa (0.075 mmHg; 0.075 Torr; 9.9 x10^-5 atm) at ambient temperature (20C-25C) and may be considered for less volatile compounds that are heated during processing/operations.

5.4 ORGANIC LIQUIDS

Liquids that are only slightly volatile or are non-volatile are assessed only for eye or skin irritancy and/or skin absorption. Volatile liquids are assessed as both liquid (eye and skin) and vapor (eye and respiratory) hazards. A chemical that is a respiratory hazard can cause respiratory irritation, or it may be absorbed from the lung into the bloodstream and cause systemic effects such as liver or kidney injury. The potential for a liquid to be a vapor hazard is determined from its amount and its vapor pressure. For example, if the vapor pressure of a liquid is low and it is not likely to escape into an inaccessible area, it is assumed that the crew would be able to remove it with an absorbent material (such as towels) before a hazardous amount of vapor is released. Therefore, it would only be a liquid hazard.

5.5 ALDEHYDE FIXATIVES

Formaldehyde (FA), paraformaldehyde (PFA), and glutaraldehyde (GA) solutions are common biological fixatives used in payload experiments. PFA is a polymer of FA and is a solid. In neutral solutions, PFA exists in equilibrium with its dissociated form, FA. All three aldehydes are very irritating to the eyes. The eye irritancy of GA at different concentrations, as reported by the Union Carbide Corporation, is shown in Appendix C. The JSC flight surgeons and toxicologists agree that solutions of FA or GA at concentrations between 0.25% and 1% are level one (THL = 1, critical) eye hazards. FA or GA concentrations ≥1% are level 2 (THL = 2, catastrophic) eye hazards.

Aldehyde solutions are volatile, and therefore, the vapor hazard must also be considered and evaluated as noted in Section 4.3. Standard vehicle volumes of dilution by Program are applied and resulting concentrations < 1 ppm are assessed as THL 0, concentrations between 1-14 ppm are assessed as THL 1, and concentrations greater than 14 ppm are assessed as THL 4 due to concerns for severe irritation that may impair the crew's ability to escape (see JSC Toxicology memorandum TOX-VR-2022-05 or most current revision). In specific situations, Programs may request vehicle-specific assessments in addition to standardized volumes.

5.6 ACIDS, BASES, AND BUFFER SOLUTIONS

Strong acids and bases are corrosive and can cause severe irritation and permanent damage to the eyes. Table 2 provides hazard levels for ocular exposure based on pH. Buffered solutions of acids and bases are more irritating than unbuffered solutions of the same pH. At the same concentration in water, a strong acid (e.g. hydrogen chloride, HCl; sulfuric acid, H_2SO_4), which is fully ionized to produce a low pH solution, is more corrosive to the surface of the eye than a weak acid (e.g. acetic acid, CH_3COOH), which is only partially ionized and produces a higher pH solution. However, the non-ionized (lipophilic) species, which can penetrate the intact corneal epithelium, is capable of causing damage to the inner structures of the eyes. The epithelium provides a barrier to charged ions and large molecules; however, if the epithelial layer is damaged (e.g. by a strong acid), the underlying structure is vulnerable to damage by the acid. Generally, at the same pH, weak organic acids (e.g. acetic acid) are more injurious to the eye than strong inorganic acids, such as HCl. Therefore, the potential eye hazards of acids are evaluated case by case. Appendix D contains information on the pH of some common acids and bases. If no toxicity information is available on the acid or base, the default hazard levels listed in Table 2 will be used.

TABLE 2 EYE HAZARD ASSESSMENTS BASED ON PH LEVELS

Hazard level	Acids (Inorganic)	Acidic Buffers (organic)	Bases	Basic Buffers
0*	> 3	> 5	<10	<9.5
1	2.1-3.0	2.6 - 5.0	10.0 - 11.4	9.5 - 10.9
2	≤2.0	≤2.5	≥11.5	≥ 11

*Neutral, weakly acidic, and weakly basic solutions are assessed a hazard level 0 (non-hazard) provided that they are not highly reactive, toxic or hypertonic (see Salt Solutions, below).

5.7 SALT SOLUTIONS

Hazards from salt solutions can be due to their hypertonicity, corrosiveness, or idiopathic toxicity. Hypertonic salt solutions can cause eye discomfort. Isotonic saline contains 155 mM (310 mOsm, or 0.9%) NaCl. Seawater, containing approximately 0.5 M (3%) NaCl, can produce transient, mild eye discomfort in some individuals. A salt concentration greater than 1 M or 2 Osm (twice that of seawater) is therefore rated a toxicity level one (THL = 1, critical) eye hazard. When very small volumes (< 5 μL) are being assessed, dilution into the fluid volume of the eye (~4 μL) may be considered. Some chemically reactive salts induce eye irritation or injury because they are strong oxidizers, (e.g. sodium hypochlorite or potassium permanganate, or reducers, e.g. hydrazine). Certain chemicals have very specific affinity for and toxicity to the eye. For example, cobalt chloride can cause injury to the eye when it is applied topically to the eye or given systemically. Because of these considerations, hazard levels are evaluated on a case-by-case basis for each solution. The reference book, *Toxicology of the Eye (W. M. Grant, 1986, Thomas Books),* is often used in assessing chemical irritancy.

5.8 GLOBALLY HARMONIZED SYSTEM (GHS) CLASSIFICATION OF OCULAR AND SKIN HAZARDS

In the absence of test data, the GHS hazard codes will be used to assign THLs per the table below.

TABLE 3 THL BY GHS CLASSIFICATION

GHS Hazard Class/Cat	GHS Hazard Statement Code	GHS Description of Hazard Statement	Corresponding NASA THL
Eye Damage and/or Irritation			
Category 1	H318	Causes serious eye damage	THL = 2
Category 2/2A	H319	Causes serious eye irritation	THL = 1
Category 2B	H320	Causes eye irritation	THL = 0
Skin Damage and/or Irritation			
Category 1	H314	Causes severe skin burns and eye damage	THL = 2
Category 2	H315	Causes skin irritation	THL = 1
Category 3	H316	Causes mild skin irritation	THL = 0

5.9 CULTURE MEDIA FOR ANIMAL AND PLANT CELLS, WHOLE PLANTS AND SMALL AQUATIC ANIMALS

Culture media for living organisms or cells generally contain nontoxic salts, nutrients, vitamins, trace minerals, buffering agents, and trace amounts of pH indicator. These solutions are generally neutral or slightly basic or acidic; the osmolarity of the solutions is usually compatible with life (i.e. not strongly hypertonic). Therefore, such media are generally assessed as level zero (THL = 0, non-hazardous). A standard culture medium may contain a long list of ingredients; the name of the medium, rather than the list of ingredients may be listed in the HMST.

5.10 CARCINOGENIC COMPOUNDS

It is rare that sufficient data exist on a given chemical to permit calculation of risk levels for carcinogenesis, particularly for relatively brief exposures. Generally, JSC Toxicology assumes that the increased risk of cancer due to brief exposures to most carcinogens is negligible, in the amounts generally used in payload experiments. For brief exposures, acute toxicity is generally a greater concern than carcinogenicity. If the calculated 180-d exposure concentration is less than the 180-d SMAC for this compound, then the chemical or test material would be rated a THL of zero (0). If a SMAC has not been established, then the life-time industrial exposure values (e.g. from the OSHA PEL, ACGIH's TLV or NIOSH's REL), will be used for assessments. If the calculated concentration of the chemical or test material is less than the lowest of these lifetime exposure values, then the chemical or test material will be rated a THL of zero (0). If the chemical or test material is not rated a THL of zero (0) then the following relative risk guidelines will be followed when it is possible to quantify the increased risk of cancer due to defined exposures.

Catastrophic: Increase in cancer risk greater than or equal to 1%

Critical: Increase in cancer risk of 0.01% up to 1%

For carcinogenic effects with a threshold, approaches such as benchmark dose modeling will be used; however, in the absence of mechanistic data, the conservative linearized multistage model will continue to be used. When benchmark dose modeling is used, only fully validated tools will be used according to the associated guidance for performing and evaluating models within those tools.

5.11 BIOLOGICAL MATERIALS

Most biological materials are not assessed from a toxicological perspective; however, some, like proteolytic enzymes or bodily fluids with extremely low pH like vomitus, may be evaluated for potential eye injury. All biological materials (e.g. live animals, plants, cultured cells,

microorganisms, viruses) as well as components or derived by-products of these (e.g. cultured cells, proteins, plasmids) will be assigned a BioSafety Level (BSL) in eHMST by JSC Microbiology.

5.12 RADIOACTIVE MATERIALS

Radioactive materials are assessed by JSC Toxicology for effects other than radiological effects (e.g. irritation effects). Information on radioactive sources is provided separately to the JSC Space Radiation Analysis Group (SRAG) in Form 44. Radiological effects are assessed, and radioactive sources are approved for flight by SRAG.

5.13 TOXICOLOGICAL ASSESSMENT OF PHARMACEUTICALS AND RESEARCH CHEMICALS

The biomedical hazard to crew member test subjects resulting from intentional administration of drugs, plasma expanders, diagnostic agents, radioactive markers, respiratory gases or other chemicals is evaluated by the IRB. JSC Toxicology evaluates the toxic hazard potential (mainly eye irritancy) of compounds or solutions if they should escape their containment. Gaseous compounds are assessed as described in Section 4.3.

Toxicology assessments usually do not include the pharmacological adverse effects (side effects and contraindications) of medications in the crew formulary. However, unintended exposures to crew medications or pharmaceutical agents in payloads (e.g. overexposures, accidental injections, secondary exposure from reclaimed resources, etc.) are assessed when appropriate.

The contents of personal medical kits for crewmembers are reviewed for potential toxicologic hazard in the event of a release. The review is performed by a designated member of the Toxicology Group, and the information is housed in a password-protected database to ensure confidentiality. For pharmaceuticals, capsules and tablets are regarded as solids and thus are not assigned a THL (i.e., “NA”).

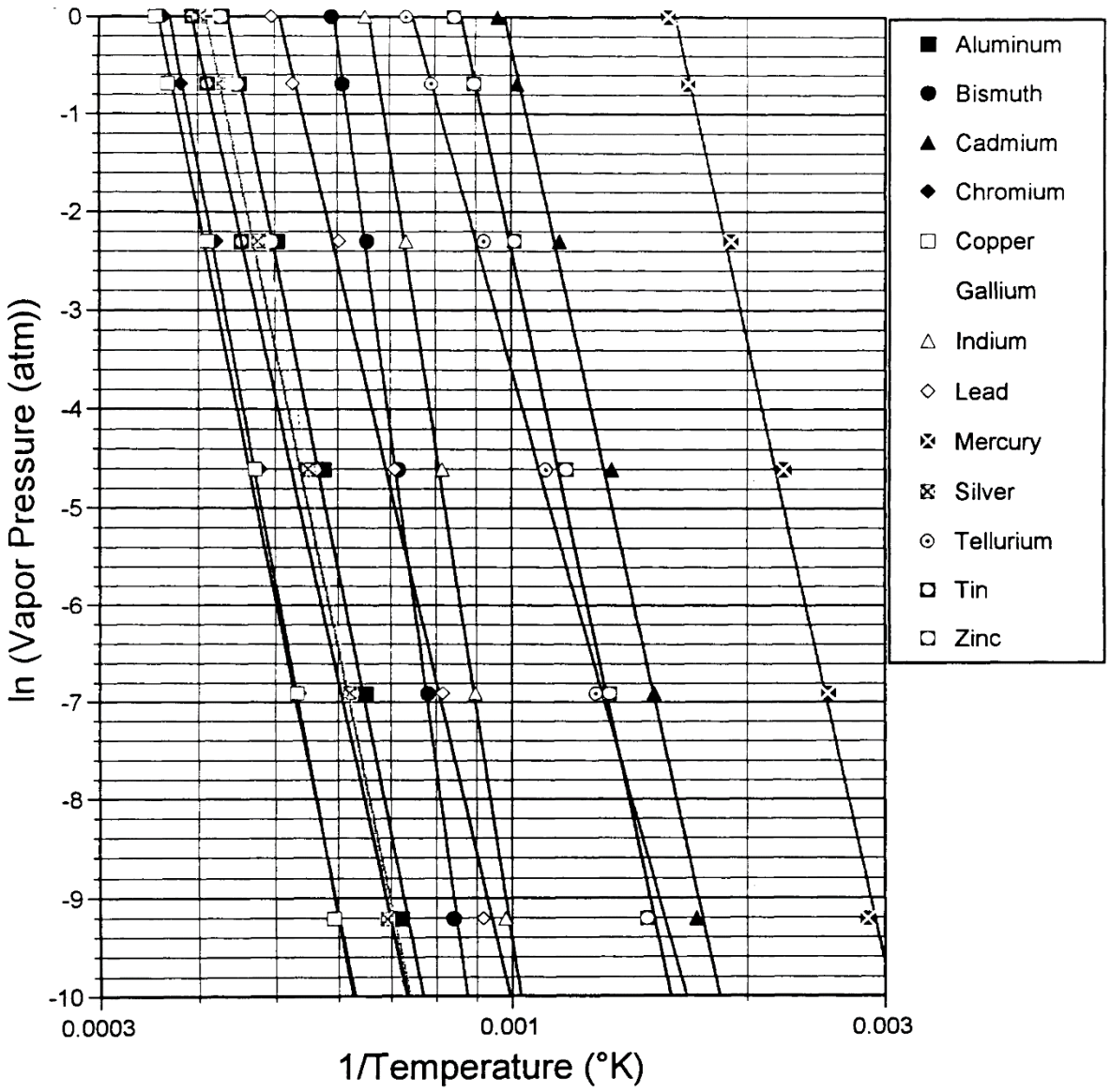
5.14 FLAMMABLE CHEMICALS

The flammability hazard of large amounts of organic materials, materials with high volatility or those with appreciable explosive potential will be assessed by the JSC Materials and Processes Branch per JSC 64825A *Guidelines for Assessing the Flammability Hazard of Spacecraft Chemicals and Test Materials*. From a flammability perspective, metals, most particulates, aqueous solutions, and organic compounds of low volatility will usually be rated as level zero (e.g. flammability = 0).

APPENDIX A. ACRONYMS AND ABBREVIATIONS

ACGIH	American Conference of Governmental Industrial Hygienists
ARS	Atmospheric Revitalization System
BME	Biomedical Flight Controller/Engineer
ECLSS	Environmental Control and Life Support System
EPA	United States Environmental Protection Agency
FA	Formaldehyde
GA	Glutaraldehyde
GFE	Government Furnished Equipment
HMST	Hazardous Materials Summary Table
HRPPC	Human Research Policy and Procedures Committee *(now called the IRB)*
IRB	Institutional Review Board *(replaced the HRPPC at JSC)*
JSC	Lyndon B. Johnson Space Center
MSDS	Material Safety Data Sheet
N/A	Not Applicable
NASA	National Aeronautics and Space Administration
NIOSH	National Institute for Occupational Safety and Health
OSHA	Occupational Safety and Health Administration
Osm	Osmolar
PEL	Permissible Exposure Limit
PFA	Paraformaldehyde
PSRP	Payload Safety Review Panel
REL	Recommended Exposure Limit
SDS	Safety Data Sheet
SMAC	Spacecraft Maximum Allowable Concentration
SRP	Safety Review Panel
THL	Toxic Hazard Level
TLV	Threshold Limit Value

APPENDIX B. CURVES OF VAPOR PRESSURE VERSUS TEMPERATURE FOR VARIOUS METALS


Curves of Vapor Pressure versus Temperature for Various Metals
ln (Vapor Pressure (atm))
0
-1
-2
-3
-4
-5
-6
-7
-8
-9
-10
0.0003
0.001
0.003
1/Temperature (°K)
Aluminum
Bismuth
Cadmium
Chromium
Copper
Gallium
Indium
Lead
Mercury
Silver
Tellurium
Tin
Zinc

APPENDIX C. SUMMARY OF THE PRIMARY IRRITANT EFFECTS OF VARIOUS CONCENTRATIONS OF GLUTARALDEYDE

Summary of the Primary Irritant Effects of Various Concentrations of Glutaraldehyde

From Union Carbide's Material Safety Data Sheet for Glutaraldehyde: "Review of Toxicological Studies and Human Health Effects" (1986).

Summary of primary irritant effects of various concentrations of glutaraldehyde on the rabbit eye: six animals per group

Glutaraldehyde Concentration, % w/w	Volume Instilled, ml	Observations
5.0	0.1	Persistent severe keratitis, corneal neovascularization, severe necrotizing blepharitis and conjunctivitis.
	0.01	Delayed onset minor to moderate corneal injury with moderate to marked conjunctivitis, persisting for 2 to 3 weeks.
	0.005	Minor transient (24 hr) corneal injury with moderate to marked conjunctivitis persisting for up to 2 weeks.
2.0	0.1	Minor corneal injury at 2 to 3 days, with moderate to marked conjunctivitis persisting for 2 to 3 weeks.
	0.01	Moderate conjunctivitis of about 3 days duration, but no corneal injury.
	0.05	Minor to moderate conjunctivitis of about 3 days duration without corneal injury.
1.0	0.1	Minor corneal injury at 2 to 7 days with moderate to marked conjunctivitis persisting for up to 2 weeks.
	0.01	Minor to moderate conjunctivitis of 2 to 3 days duration without corneal injury.
0.5	0.1	Mild injection of conjunctiva of 48 hours duration. No corneal injury.
	0.01	Minimal injection of conjunctivae of less than 24 hours duration. No corneal injury.
0.2	0.1	Minimal injection of conjunctivae of 24 hours duration. No corneal injury.
	0.01	No effects.
0.1	0.1	No effects.
	0.01	No effects.

APPENDIX D. ACIDITY AND ALKALINITY OF SOME COMMON LIQUIDS

Acidity and Alkalinity of Some Common Liquids

APPROXIMATE pH values

The following tables give approximate pH values for a number of substances such as acids, bases, foods, biological fluids, etc. All values are rounded off to the nearest tenth and are based on measurements made at 25 °C. A few buffer systems with their pH values are also given.

From Handbook of Chemistry and Physics, CRC Press, 65th edition, page D-150:
Modern pH and Chlorine Control, W. A. Taylor & Co.

ACIDS

Hydrochloric, N	0.1	Oxalic, 0.1N	1.6	Acetic, 0.01N	3.4
Hydrochloric, 0.1N	1.1	Tartaric, 0.1N	2.2	Benzoic, 0.01N	3.1
Hydrochloric, 0.01N	2.0	Malic, 0.1N	2.2	Alum, 0.1N	3.2
Sulfuric, N	0.3	Citric, 0.1N	2.2	Carbonic (saturated)	3.8
Sulfuric, 0.1N	1.2	Formic, 0.1N	2.3	Hydrogen sulfide, 0.1N	4.1
Sulfuric, 0.01N	2.1	Lactic, 0.1N	2.4	Arsenious (saturated)	5.0
Orthophosphoric, 0.1N	1.5	Acetic, N	2.4	Hydrocyanic, 0.1N	5.1
Sulfurous, 0.1N	1.5	Acetic, 0.1N	2.9	Boric, 0.1N	5.2

BASES

Sodium hydroxide, N	14.0	Lime (saturated)	12.4	Magnesia (saturated)	10.5
Sodium hydroxide, 0.1N	13.0	Trisodium phosphate, 0.1N	12.0	Sodium sesquicarbonate, 0.1M	10.1
Sodium hydroxide, 0.01N	12.0	Sodium carbonate, 0.1N	11.6	Ferrous hydroxide (saturated)	9.5
Potassium hydroxide, N	14.0	Ammonia, N	11.6	Calcium carbonate (saturated)	9.4
Potassium hydroxide, 0.1N	13.0	Ammonia, 0.1N	11.1	Borax, 0.1N	9.2
Potassium hydroxide, 0.01N	12.0	Ammonia, 0.01N	10.6	Sodium bicarbonate, 0.1N	8.4
Sodium metasilicate, 0.1N	12.6	Potassium cyanide, 0.1N	11.0		

BIOLOGIC MATERIALS

Blood, plasma, human	7.3–7.5	Gastric contents, human	1.0–3.0	Milk, human	6.6–7.6
Spinal fluid, human	7.3–7.5	Duodenal contents, human	4.8–8.2	Bile, human	6.8–7.0
Blood, whole, dog	6.9–7.2	Feces, human	4.6–8.4		
Saliva, human	6.5–7.5	Urine, human	4.8–8.4		

FOODS

Apples	2.9–3.3	Gooseberries	2.8–3.0	Potatoes	5.6–6.0
Apricots	3.6–4.0	Grapefruit	3.0–3.3	Pumpkin	4.8–5.2
Asparagus	5.4–5.8	Grapes	3.5–4.5	Raspberries	3.2–3.6
Bananas	4.5–4.7	Hominy (lye)	6.8–8.0	Rhubarb	3.1–3.2
Beans	5.0–6.0	Jams, fruit	3.5–4.0	Salmon	6.1–6.3
Beers	4.0–5.0	Jellies, fruit	2.8–3.4	Sauerkraut	3.4–3.6
Beets	4.9–5.5	Lemons	2.2–2.4	Shrimp	6.8–7.0
Blackberries	3.2–3.6	Limes	1.8–2.0	Soft drinks	2.0–4.0
Bread, white	5.0–6.0	Maple syrup	6.5–7.0	Spinach	5.1–5.7
Butter	6.1–6.4	Milk, cows	6.3–6.6	Squash	5.0–5.4
Cabbage	5.2–5.4	Olives	3.6–3.8	Strawberries	3.0–3.5
Carrots	4.9–5.3	Oranges	3.0–4.0	Sweet potatoes	5.3–5.6
Cheese	4.8–6.4	Oysters	6.1–6.6	Tomatoes	4.0–4.4
Cherries	3.2–4.0	Peaches	3.4–3.6	Tuna	5.9–6.1
Cider	2.9–3.3	Pears	3.6–4.0	Turnips	5.2–5.6
Corn	6.0–6.5	Peas	5.8–6.4	Vinegar	2.4–3.4
Crackers	6.5–8.5	Pickles, dill	3.2–3.6	Water, drinking	6.5–8.0
Dates	6.2–6.4	Pickles, sour	3.0–3.4	Wines	2.8–3.8
Eggs, fresh white	7.6–8.0	Pimento	4.6–5.2		
Flour, wheat	5.5–6.5	Plums	2.8–3.0		