RADIATION RISK ACCEPTABILITY AND LIMITATIONS

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ACCEPTABLE LEVELS OF RISKS – HISTORICAL PERSPECTIVE

Permissible exposure limits (PEL) for radiation exposure of astronauts have the primary functions of preventing in-flight risks that would jeopardize mission success and limiting chronic risks to acceptable levels based on legal, ethical or moral, and financial considerations. Early radiation effects usually are related to a significant fraction of cell loss, exceeding the threshold for impairment of function in a tissue. These are "deterministic" effects, so called because the statistical fluctuations in the number of affected cells are very small compared to the number of cells required to reach the threshold (ICRP 1991). Maintaining dose limits can ensure that no occurrence of early effects occurs. Late effects can result from changes in a very small number of cells, so that statistical fluctuations can be large and some level of risk is incurred even at low doses. Referring to them as a "stochastic" effect recognizes the predominance of statistical effects in their manifestation.

NASA has followed several distinct recommendations on radiation limits since the Apollo era today due to the evolving understanding of space radiation environments inside spacecraft and tissue, new epidemiology data, and the age and gender makeup of astronauts. Recommendations by the National Academy of Sciences (NAS) in 1967 (NAS 1967) noted that radiation protection in manned space flight is philosophically distinct from protection practices of terrestrial workers because of the high-risk nature of space missions. The 1967 NAS report did not recommend "permissible doses" for space operations, noting the possibility that such limits may place the mission in jeopardy and instead made estimates of what the likely effects would be for a given dose of radiation (Schimmerling, 2009).

In 1970, the NAS Space Science Board made recommendations for guidelines for career doses to be used by NASA for long-term mission design and manned operations. At that time, NASA employed only male astronauts and the typical age of astronauts was 30-40 years. A "primary reference risk" was proposed equal to the natural probability of cancer over a period of 20-years following the radiation exposure (using the period from 35 to 55 years of age) and was essentially a doubling dose. The estimated doubling dose of 382 rem (3.82 Sv), which ignored a dose-rate reduction factor, was rounded to 400 rem (4 Sv). The NAS panel noted that their recommendations were not risk limits, but rather a reference risk and that higher risk could be considered for planetary missions or a lower level of risk for a possible space station (NAS 1970). Ancillary reference risks were described to consider monthly, annual, and career exposure patterns. However, the 1970 NAS recommendations were implemented by NASA as dose limits used operationally for all missions until 1989.

At the time of the 1970 NAS report the major risk from radiation was believed to be leukemia. Since that time the maturation of the data from the Japanese atomic bomb (AB)

survivors has led to estimates of higher levels of cancer risk for a given dose of radiation including the observation that the risk of solid tumors following radiation exposure occurs with a higher probability than leukemia's although with a longer latency period before expression. Along with the maturation of the AB data, re-evaluation of the dosimetry of the AB survivors, and inclusion of data from other exposure cohorts, scientific assessments of the dose response models and dose-rate dependencies have contributed to the large increase in the risk estimate over this time period (1970-2009)**,** and these continue to be modified (BEIR 2006; UNSCEAR 2006). A newer finding is the large risk of heart disease death from radiation that appears in many exposed cohorts (Little et al., 2010), albeit data for low dose-rate exposures is inconsistent. The mortality risk for heart disease may approach that of solid cancers at least at older ages (Preston et al. 2003) and research in this area will be important in the future.

By the early 1980's several major changes had occurred leading to the need for a new approach to define dose limits for astronauts. At that time NASA requested the U.S. National Council on Radiation Protection and Measurements (NCRP) to re-evaluate dose limits to be used for LEO operations. Considerations included the increases in estimates of radiation-induced cancer risks in the Japanese A-bomb survivors, the criteria for risk limits, and the role of the evolving makeup of the astronaut population from male test pilots to a larger diverse population (~100) astronauts including mission specialists, female astronauts, and career astronauts of older ages who often participate in several missions. In 1989, the NCRP Report No. 98 recommended age and gender dependent career dose limits using a 3% increase in cancer mortality as a common risk limit. The limiting level of 3% excess cancer fatality risk was based on several criteria including comparison to dose limits for ground radiation workers and to rates of occupational death in the less-safe industries. It was noted that astronauts face many other risks and adding an overly large radiation risk was not justified. It also is noted that the average years of life loss from radiation induced cancer death, about 15 years for workers over age 40-y, and 20 years for workers between 20-40 y, is less than that of other occupational injuries. A comparison of radiation-induced cancer deaths to cancer fatalities in the US population is also complex because of the smaller years of life loss from cancers in the general population where most cancer deaths occur above age 70-y.

In the 1990's, the additional follow-up and evaluation of the AB survivor data led to further increases in the estimated cancer risk for a given dose of radiation. Recommendations from the NCRP (NCRP, 2000), while keeping the basic philosophy of risk limitation in their earlier report, advocated significantly lower limits than those recommended in 1989 (NCRP, 1989). The NCRP Report No. 132 (NCRP 2000) notes that the use of comparisons to fatalities in the less-safe industries advocated by the NCRP in 1989 was no longer viable because of the large improvements made in ground-based occupational safety; indeed, the decreased rate of fatalities in the so-called less safe industries, such as mining and agriculture, would suggest a limit well below the 3% fatality level estimated in 1989. The most recent reviews of the acceptable levels of radiation risk for LEO, including a 1996 NCRP symposium (NCRP 1997a) and the report on LEO dose limits from the NCRP (NCRP 2000), instead advocate that comparisons to career dose limits for ground-based workers should be used. On the one hand, it is widely

held that the social and scientific benefits of space flight continue to provide justification for the 3% risk level for astronauts participating in exploration missions. On the other hand, improvements in other aspects of space safety (NASA 2009) place pressure for improvement in radiation protection. The recent report from the National Research Council (NRC) (NRC 2008) reinforces the need to uphold radiation limits at NASA for safe mission design and astronaut health.

In comparison to NASA limits, the US nuclear industry has adopted age-specific limits that neglect any gender dependence. Limits are set at an Effective dose equal to the individuals Age × 0.01 Sv. It is estimated by the NCRP that ground workers who reach their dose limits would have a lifetime risk of about 3%, but note the differences in dose values corresponding to the limit due to differences in how the radiation doses are accumulated over the worker's career. NASA's short-term LEO dose limits are several times higher than those for terrestrial workers because they are intended to prevent acute risks, while annual dose limits of 50 mSv (5 rem) allowed for US terrestrial radiation workers are intended to control the accumulation of career doses. The exposures received by radiation workers in reactors, accelerators, hospitals, etc. rarely approach dose limits with the average annual exposure of 1 to 2 mSv, which is a factor of 25 below the annual exposure limit, and significantly less than the average Effective dose of 80 mSv for 6-month ISS missions (Cucinotta et al., 2008). Similarly, transcontinental pilots, although not characterized as radiation workers in the United States, receive annual exposures of about 1 to 5 mSv and enjoy long careers without approaching exposure limits recommended for terrestrial workers in the US. Under these conditions, ground-based radiation workers are estimated to be well below the career limits, even if a 95% confidence level is applied. Because space missions have been relatively short in the past requiring minimal mitigation consideration, the impact of dose limits when space programs actually approach such boundaries including the application of the ALARA principle has been unexplored.

Late occurring morbidity risks associated with space radiation are difficult to compare to other occupational risks. Traditionally, radiation mortality risks have been used as the primary criteria for setting career risk limits. For example, basal cell carcinomas of the skin and thyroid cancers are more easily treated than leukemias or lung and breast cancers, which involve a larger degree of suffering and costs. The NCRP (1989) has used the quantity of excess risk of cancer mortality to estimate age- and gender-dependent dose limits, which differ from the Risk of Exposure Induced Death (REID). The excess risk is a calculation of the increased risk above the background level of cancer deaths in a population not exposed to radiation and does not account for cancer deaths that would occur anyway, but are shifted to an earlier age due to radiation exposure. The REID quantity accounts for these deaths and when supplemented with estimates of years of life-loss for deaths occurring , it is a more meaningful comparison to other mortality risks of astronauts.

Summary of Approaches for Setting Acceptable Levels of Risk

The various approaches to setting acceptable levels of radiation risks are summarized here:

1. *Unlimited Radiation Risk:* NASA management and the families or loved ones of astronauts would find this approach unacceptable.
2. *Comparison to Occupational Fatalities in Less-Safe Industries*: The life-loss from attributable radiation cancer death is less than from most other occupational deaths. Also, at this time this comparison would be very restrictive for ISS operations or for lunar and Mars missions because of continued improvements in ground-based occupational safety over the last 20 years.
3. *Comparison to Cancer Rates in General Population:* The life-loss from radiation-induced cancer can be significantly larger than from cancer deaths in the general population, which often occur late in life >70-y.
4. *Doubling dose for 20-yrs following exposure:* Provides a roughly equivalent comparison base of life-loss from other occupational risks or background cancer fatalities during the worker's career. However, this negates the role of mortality later in life.
5. *Use of Ground-based worker limit of ~3% or similar approach:* Provides a reference point equivalent to standards set on Earth and recognizes that astronauts face other risks. However, ground workers remain well below dose limits and are largely exposed to low-LET radiation, whereas uncertainties from biological effects are much smaller than those for space radiation.

NASA'S PERMISSIBLE EXPOSURE LIMITS

We next summarize the radiation limits at NASA to be used for exploration missions.

Cancer Risk Limits: Career exposure to radiation is not to exceed 3% risk of exposure induced death (REID) from fatal cancers. An ancillary requirement assures that this risk limit is not exceeded at a 95% confidence level using a statistical assessment of the uncertainties in the risk projection calculations to limit the cumulative Effective dose (in units of Sievert) received by an astronaut throughout his or her career.

Cancer Risk to Dose Relationship: The relationship between radiation exposure or dose and risk is age and gender specific due to latency effects, differences in tissue types and sensitivities, and differences in average life spans between genders**.** These relationships are estimated using the double detriment life-table methodologies recommended by the NCRP (2000) and more recent radiation epidemiology information (Preston et al., 2003; Cucinotta et al., 2006). **Table 1** lists examples of career Effective dose (E) limits for a REID=3% for missions of 1-year duration or less. Limits for other mission lengths will vary and should be calculated using the appropriate life-table formalism. Note the values in **Table 1** differ from the values typically quoted for 10-year careers (NCRP 1989, 2000) since cancer risk will decrease with age at exposure. Estimates of average life-loss for a

radiation attributable death based on low LET radiation are also listed in **Table 1**; however, higher values should be expected for high LET exposures such as GCR.

Table 1. Example career Effective dose limits for 1-year missions for a 3% REID and estimates of average life-loss if death occurs.

	E(mSv) for a 3% REID (Ave. Life-loss per Death, y)	
Age at Exposure, y	**Males**	**Females**
30	620 (15.7)	470 (15.7)
35	720 (15.4)	550 (15.3)
40	800 (15.0)	620 (14.7)
45	950 (14.2)	750 (14.0)
50	1150 (12.5)	920 (13.2)
55	1470 (11.5)	1120 (12.2)

Dose Limits for Non-Cancer Effects: Short-term dose limits are imposed to prevent clinically significant non-cancer health effects including performance degradation, sickness, or death in-flight. For risks that occur above a threshold dose, a probability of $<10^{-3}$ is a practical limit. However, radiobiology data rarely determine risk probability < 10^{-2}. The dose limits for the blood forming organs (BFO) should be adequate to project against the risks of prodromal effects such as nausea, vomiting, and fatigue. Dose limits for cataracts, skin, heart disease, and damage to the central nervous system (CNS) are imposed to limit or prevent risks of degenerative tissue diseases (e.g., stroke, coronary heart disease, striatum aging or dementia, etc.) that could occur post-mission. Career limits for the heart are intended to limit the REID for heart disease to be below a few percent, and are expected to be largely age and gender independent. Dose limits for non-cancer effects (units of milli-Gray Equivalent (mGy-Eq)) are listed in **Table 2**. Distinct relative biological effectiveness (RBE) factors for converting organ average dose to organ Gy-Equivalent dose occur for each non-cancer risk as defined below. CNS risks are expressed as mGy-Equivalent dose; however, with a separate limit for heavy ions with elemental charge >10 absorbed dose (in mGy).

Table 2. Dose limits for Short-term or Career Non-Cancer Effects (in mGy-Eq. or mGy).

Organ	**30-day Limit**	**1 Year Limit**	**Career Limit**
Lens*	1000 mGy-Eq	2000 mGy-Eq	4000 mGy-Eq
Skin	1500	3000	6000
BFO	250	500	Not applicable
Heart**	250	500	1000
CNS***	500	1000	1500
CNS*** ($Z \geq 10$)	-	100 mGy	250 mGy

***Lens limits are intended to prevent early (<5 yr) severe cataracts (e.g., from a solar particle event). An additional cataract risk exists at lower doses from cosmic rays for sub-clinical cataracts, which may progress to severe types after long latency (>5 yr) and are not preventable by existing mitigation measures. However, they are deemed an acceptable risk by NASA.**

****Heart doses calculated as average over heart muscle and adjacent arteries.**

*****CNS limits should be calculated at the hippocampus.**

The Principle of As Low as Reasonably Achievable (ALARA): The ALARA principle is a NASA requirement intended to ensure astronauts safety. An important function of ALARA is to ensure that astronauts do not approach radiation limits and that such limits are not considered as "tolerance values." Mission programs and terrestrial occupational procedures resulting in radiation exposures to astronauts are required to find cost-effective approaches to implement ALARA.

Radiation Limits for Other Space Agencies

The European Space Agency (ESA), Russian Space Agency (RSA), and Japanese Space Agency (JAXA) use dose limits for astronauts and cosmonauts largely based on the recommendations of the International Commission on Radiological Protection (ICRP) for ground-based works with some modifications for 30-day and annual limits for non-cancer effects. A series of flight rules and action levels is in place for the ISS based on real-time dosimetry, mission length, and prior crew exposures. Crew are not selected for missions if they are projected to exceed career limits at the end of any given mission.

Table 3. ESA Dose Limits

Limit	Value	Comment
Career	1 Sv (1000 mSv)	ICRP- no age or gender dependence
Blood Forming Organs (BFO)	0.25 Sv for 30 d; 0.5 Sv for Annually	ISS Consensus limits
Eye	0.5 Sv for 30 d; 1.0 Sv Annually	
Skin	1.5 Sv for 30 d 3.0 Sv for Annually	

The Russian Space Agency (RSA) uses the following Dose limits.

Table 4. RSA Dose Limits

Limit	Value	Comment
Career	1 Sv (1000 mSv)	ICRP- no age or gender dependence
Blood Forming Organs (BFO)	0.15 Sv for Acute (1-time) 0.25 Sv for 30 d; 0.5 Sv for Annually	
Eye	0.5 Sv for 30 d; 1.0 Sv Annually 2.0 Sv for Career	
Skin	1.5 Sv for 30 d 3.0 Sv for Annually 6.0 Sv for Career	

Method of Evaluation of Organ Dose Equivalents

Cancer Risk Evaluation: Cancer risk is not measured directly, but is calculated utilizing radiation dosimetry, physics methods, and dose to risk conversion formula. The absorbed dose D (in units of Gray) is calculated using measurements of radiation levels provided by dosimeters (e.g., film badges, thermoluminescent dosimeters (TLDs), spectrometers such as the tissue equivalent proportional counter (TEPC), area radiation monitors, biodosimetry or biological markers) and corrections for instrument limitations. The limiting risk is calculated using the Effective dose, *E* (in units of mSv) and risk conversion life-table methodologies. For the purpose of determining radiation exposure limits at NASA, the probability of fatal cancer is calculated as follows:

1. The body is divided into a set of sensitive tissues, and each tissue *T* is assigned a weight w_T according to its estimated contribution to cancer risk as described by the ICRP (**Table 5**).
2. The absorbed dose, D_T (in units of Gray (Gy) or mGy where 1 Gy = 100 rad) delivered to each tissue is determined from measured dosimetry or estimated from radiation transport models. Different types of radiation have different biological effectiveness, dependent on the ionization density left behind locally (e.g., in a cell or a cell nucleus) by their passage through matter. For the purpose of estimating radiation risk to an organ, the quantity characterizing this ionization density is the Linear Energy Transfer (LET) (in units of keV/μm) in water.

Table 5. Tissue weighting factors as defined by ICRP (1991 & 2007).

Tissue/Organ	ICRP w_T	
	ICRP 60 (1991)	ICRP 103 (2007)
Skin	0.01	0.01
Bone marrow	0.12	0.12
Bone surface	0.01	0.01
Stomach	0.12	0.12
Colon	0.12	0.12
Liver	0.05	0.04
Lung	0.12	0.12
Esophagus	0.05	0.04
Bladder	0.05	0.04
Thyroid	0.05	0.04
Breast or Prostate	0.05	0.12
Ovary + Uterus, or Testis	0.2	0.08
Brain		0.01
Lens		
Salivary gland		0.01
Remainder	0.05*	0.12**
Sum	1	1

*Remainder organ/tissue defined in ICRP 60: adrenals, brain, trachea, small intestine, kidneys, muscle, pancreas, spleen, thymus and uterus.
**Remainder organ/tissue defined in ICRP 103: adrenals, extrathoracic (ET) region, gall bladder, heart, kidneys, lymphatic nodes, muscle, oral mucosa, pancreas, prostate, small intestine, spleen, thymus, uterus/cervix.

3. For a given interval of LET, denoted L, between L and $L+\Delta L$, the dose equivalent risk (units of Sievert (Sv) or mSv, where 1 Sv = 100 rem) to a tissue T, $H_T\,(L)$ is calculated as:

$$H_T(L) = Q(L)D_T(L), \quad (1)$$

where the quality factor, $Q(L)$, is obtained according to the International Commission on Radiological Protection (ICRP) prescription. This way of calculating $H_T(L)$ differs from the method used by ICRP, where a tabulated set of weighting factors is given instead of the quality factor (NCRP, 2003). The method used here is considered to yield a better approximation by using the quality factor as the weight most representative of cancer risk, while the ICRP method may overestimate the risk,

especially for high-energy protons, He, and other light to medium mass ions. Neutron contributions are evaluated by their contribution to $D_T(L)$.

4. The average risk to a tissue T, due to all types of radiation contributing to the dose, is given by:

$$H_T = \int \frac{dD_T(L)}{dL} Q(L) dL, \qquad (2)$$

or, since $dD_T(L) = L dF_T(L)$, where $F_T(L)$ is the fluence of particles with LET=L, traversing the organ,

$$H_T = \int dL Q(L) F_T(L) L. \quad (3)$$

5. The Effective dose (in units of Sv) is used as a summation over radiation type and tissue using the tissue weighting factors, w_T,

$$E = \sum_T w_T H_T. \qquad (4)$$

6. For a mission of duration t, the Effective dose will be a function of time, $E(t)$, and the Effective dose for mission i will be:

$$E_i = \int \frac{dE(t)}{dt} dt \qquad (5)$$

and in applying the associated risk factor $R_0(age_i, gender)$, age_i is the average age during the mission.

7. The Effective dose is used to scale the mortality rate for radiation-induced death from the Japanese survivor data using the average of the multiplicative and additive transfer models for solid cancers and the additive transfer model for leukemias and applying life-table methodologies based on the US population data for background cancer and all causes of death mortality rates. A dose and dose-rate reduction effectiveness factor (DDREF) of 2 is assumed to reduce cancer risks at low dose and dose-rates compared to acute radiation cancer risk.

Evaluation of Cumulative Cancer Risk: The cumulative cancer fatality risk (%REID) to an astronaut for N occupational radiation exposures is found by applying life table methodologies, which can be approximated at small values of %REID by summing over the tissue-weighted Effective dose, E_i, as:

$$Risk = \sum_{i=1}^{N} E_i R_0(age_i, gender). \qquad (6)$$

where R_0 are the age and gender specific radiation mortality rates per unit Effective dose. The Effective dose limits given in the **Table 1** illustrate the Effective dose that corresponds to a 3% REID for missions of duration up to one year. Values for multiple missions or other occupational exposure can be estimated using equation (6) or directly

from life-table calculations (Cucinotta et al. 2006). For organ dose calculations, NASA uses the model of Billings et al. (1973) to represent the self-shielding of the human body in a water equivalent mass approximation. Consideration of the orientation of the human body relative to vehicle shielding should be made if known, especially for solar particle events (Wilson et al., 1995).

Non-Cancer Risk Limits: The method used for evaluating the equivalent dose for non-cancer effects is similar to Eq. (2) or (3); however, the method uses the "Gy-Equivalent" to distinguish Effective doses based on relative biological effectiveness factors (RBE) for non-cancer effects from those based on Q-values to be used for estimating cancer risks. Tissue specific Gy-Equivalents are denoted G_T. Because RBE's for non-cancer effects may depend on dose, the RBE factors used for specifying the Gy-Equivalent are the values determined at the threshold dose for the non-cancer effect being evaluated. ICRP and NCRP recommendations for RBE values for short-term non-cancer effects are listed in **Table 6** and are generally smaller than the Q-values. Based on available radiobiology data for non-cancer late effects, organ dose-Eq estimates for cataracts, heart and CNS risks are expected to be highly uncertain.

Table 6. NCRP Recommendations on RBE values for non-cancer radiation effects to be used for skin and blood forming organ (BFO) risks[a].

Radiation Type	*Recommended RBE*[b]	*Range*
1 to 5 MeV neutrons	6.0	(4-8)
5 to 50 MeV neutrons	3.5	(2-5)
Heavy ions	2.5[c]	(1-4)
Proton > 2 MeV	1.5	-

[a]RBE values for late deterministic effects are higher than for early effects in some tissues and are influenced by the doses used to determine the RBE.

[b]There are not sufficient data on which to base RBE values for early or late effects by neutrons of energies <1 MeV or greater than about 25 MeV.

[c]There are few data for the tissue effects of ions with a Z>18 but the RBE values for iron ions (Z=26) are comparable to those of argon (Z=18). One possible exception is cataract of the lens of the eye because high RBE values for cataracts in mice have been reported.

Confidence levels for Career Cancer Risks are evaluated using the methods specified by the NCRP in their Report No. 126 (NCRP, 1997) modified to account for the uncertainty in quality factors and space dosimetry (Cucinotta et al., 2001, 2005). The uncertainties considered in the evaluation of the 95% confidence levels are:

1. The uncertainties in human epidemiology data including uncertainties in
    a. statistics limitations of epidemiology data
    b. dosimetry of exposed cohorts
    c. bias including misclassification of cancer deaths
    d. the transfer of risk across populations

2. The uncertainties in the dose- and dose-rate reduction (DDREF) factor used to scale acute radiation exposure data to low dose and dose-rate radiation exposures.
3. The uncertainties in the radiation quality factor (Q) as a function of LET.
4. The uncertainties in space dosimetry.

The so-called "unknown uncertainties" included by the NCRP (1997) are ignored. The statistical distribution for the estimated probability of fatal cancer is evaluated in order to project the most likely values and the lower and upper 95% confidence intervals (C.I) reported within brackets. For example, for the average adult exposed to 100 mSv (10 rem) of gamma-rays, the estimated cancer risk is 0.4 % and the 95% C.I.'s estimated by the NCRP are written as [0.11%, 0.82%] where 0.11% is the lower 95% level and 0.82% is the upper 95% confidence level. In order to assure that the career risk limit is not exceeded with a safety margin corresponding to a 95% confidence level, the upper confidence level (worst-case) is considered in the developing mission constraints and for crew selection. **Table 7** lists approximate fold uncertainties defined as the ratio of the upper 95% confidence level to the median project. These results summarize Monte-Carlo propagation of errors based on subjective evaluation of uncertainties in physical, biological and epidemiological factors that enter into risk projections (NCRP, 1997, Cucinotta et al., 2006).

Table 7. Approximate Fold Uncertainty defined as ratio of upper 95% Confidence Level to point risk projection.

Type of Exposure	*Approximate Ratio of upper 95% confidence interval to mean projection*
Medical Diagnostic	*2.0*
ISS Environment	*3.1*
Solar Particle Event	*2.5*
Deep Space or Planetary Surface GCR	*4.0*

Confidence levels or uncertainty factors for acute risks such as radiation sickness or mortality are manifested in the models of RBE's as function of ion type and in the dose-rate reduction and repopulation effects that modify threshold doses. The dose limit values shown in **Table 2** are expected to be conservative; however, the actual margin between the limit and a significant probability of effect ($>10^{-3}$) should be considered in determining uncertainty bounds. The shape of the dose-response function for acute risks near the threshold dose is poorly understood and will likely dependent on individual responses.

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