

Data gaps relevant to guidelines setting

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ICNIRP PG on "data gaps identified during guidelines' development

Task: Draft a research agenda for the whole NIR spectrum, based in particular on the gaps identified during guidelines development. The ICNIRP research agenda aims at identifying knowledge gaps relevant for giving protection guidance.

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PG method

- Set sub-groups for each guidelines, starting to examine those already published; Separate agenda documents will be developed for different frequency ranges, with the frequency ranges corresponding to those of the various ICNIRP Guidelines. It was agreed that where there was overlap between different frequency ranges, that such overlap would be noted in the respective documents
- Use an algorithm to identify with always the same modality the topic, the end-points, the data really weak or not investigated.

The DG-PG will develop research agendas for the following guidelines corresponding to different frequency ranges:

- Guidelines for Limiting Exposure to Time-Varying Electric and Magnetic Fields (1 Hz - 100 kHz).
- Guidelines for limiting exposure to electric fields induced by movement of the human body in a static magnetic field and by time-varying magnetic fields below 1 Hz;
- Guidelines for Optical Radiation (wavelengths 1 mm to 1 nm);
- Guidelines for Ultrasound (acoustic frequencies from 1 to 40 MHz) as soon as they are delivered;
- Guidelines for High Frequency - at the end of the development.

This PG has no 'final' deliverable, as it will continue to update research recommendations following each Guideline publication.

The algorithm was set during the first year and apply to the ELF guidelines for first.

Notes on the Data Gaps Algorithm

- Purpose
 - Maximise transparency
 - Maximise consistency across Guidelines
 - Maximise relevance to Guidelines settings
 - Provide help with the Guidelines setting process
 - Avoid recommending 'research that does not directly benefit the Guidelines setting process
- Structure
 - Two sections, addressing research concerning
 - Health effects *identified* in current Guideline
 - Health effects *not-identified* in current Guideline
- Guiding principles
 - Requires positive reasons for recommending research
 - Algorithm is to be used as a guide, and educated evaluation is final arbiter

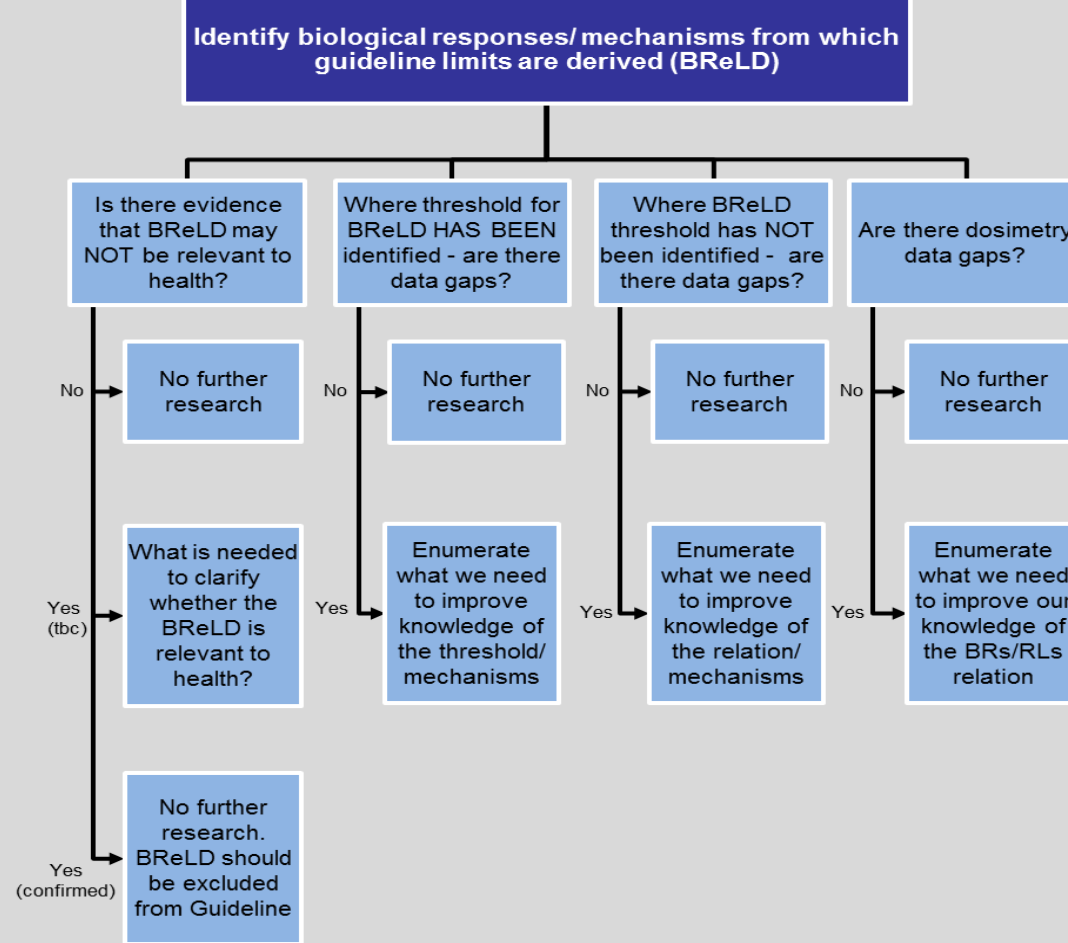
Notes on implementation of the Algorithm

1. It is important to note that although this algorithm will provide the direction and justification for the process, it is not intended to do so at the expense of the primary objective, which is to encourage research that will inform Guideline development. Thus the DG-PG is encouraged to also think outside of the structure, and to include research recommendations even if they do not fit neatly within the algorithm. Where such inconsistencies are identified between the algorithm and the research recommendations:
Justification will need to be provided as to why the research recommendations are given in spite of not satisfying the algorithm; and
A reconsideration of the algorithm will be engaged to improve its applicability for future Research Needs development.
2. Note that research developing our understanding of bioelectromagnetic interactions necessarily involves both dosimetry and biology.

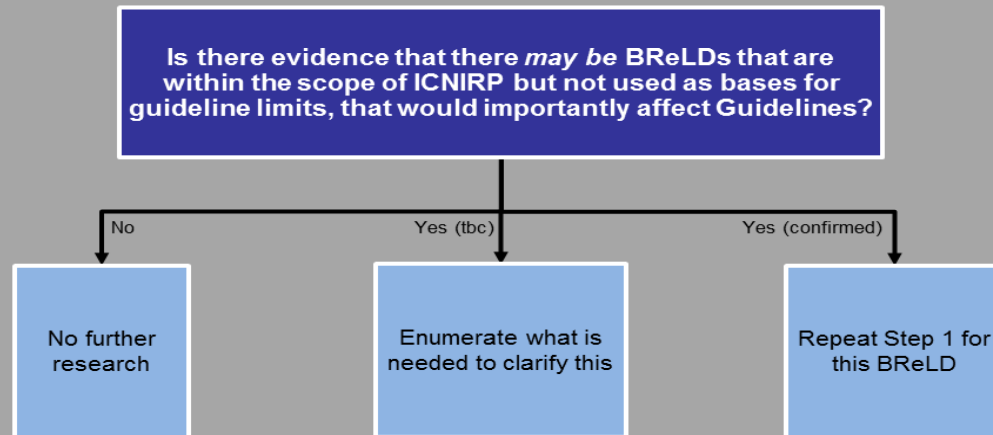
Notes on implementation of the Algorithm (2)

3. Although the research algorithm is for the purpose of highlighting research that will benefit future Guideline development, it is important to note that this is not meant to limit research more generally.
4. In deriving the research recommendations, the DG-PG should avoid duplicating effort, but rather utilise pre-existing documents as the starting point for deliberation.
5. Research recommendations do not need to be treated as hierarchical
6. Note that a range of factors are relevant to the algorithm that may not be specifically listed in the Algorithm.

1. Identify & evaluate biological responses in current Guidelines



2. Check for important health effects missing from Guidelines



ELF gaps Table (.....work in progress)

Topic	Robustness	Consistency	Final revised score
Neural Network Firing Patterns	Well established phenomena	Wide range of estimates of sensitivities	Uncertainties in precise mechanism and derivation of tissue E-fields implies that actual thresholds could be lower (or higher) than current levels
Free Radical Lifetimes	Effect of B-fields on lifetimes well-established, but at higher field values than Reference Levels	Experimental thresholds appear to be above those predicted theoretically, however fish and birds appear to be very sensitive to small variations in environmental fields (however, not so much at ELF)	Ongoing research outcomes may force revision of conclusions regarding relevance to standard-setting
Biogenic Magnetite	Existence of magnetite particles well established, although biological mechanism and significance unclear	Debate on nature of 'magnetic sensor'	As above
Neurobehaviour	Limited and heterogeneous human research showing no effect Review of animal studies showing a possible effect	Inconsistent results between human and animal data	No data gaps in human research related to guideline development. There are some positive results in animal studies which point to possible data gaps in this area
Neuroendocrine system	Very few studies	Inconsistent results	Data gaps in relation to the melatonin hypothesis and associated interaction mechanisms

ELF gaps Table 2 (...work in progress)

Topic	Robustness	Consistency	Final revised score
Neurodegenerative disorders	Many methodological problems in epidemiological research. Experimental studies not adequate.	Inconsistent results	Data gaps in further epidemiological work as well as mechanisms and biological data on experimental models
Reproduction and development	Limited research	Generally no support for reproductive outcomes	No data gaps identified for further research in relation to guideline development
Cardiovascular disorders	Limited research	Generally no support for cardiovascular disorders	No data gaps identified for further research in relation to guideline development
Childhood leukaemia	Limited research on adequate animal models	Generally no support for cancer induction or promotion	Data gaps in further mechanisms and biological data on childhood leukaemia experimental models
Dosimetry & modelling	Research database growing	Some inter-comparison between models, but more needed. More critical examination of assumptions made required	Considerable gaps remain, including disparities between the major standards

Data Gap: Optical Radiation - Introduction

Natural Sources

- The Sun
- Planckian Emitters

Artificial Sources

- Planckian Emitters
- Incandescence
- Fluorescence
- Light emitting diodes (LEDs)
- Phosphor Converted LEDs (PC LEDs)
- Lasers

Source Characteristics and Range of Possible Exposure

- Monochromatic, Polychromatic, and “Broadband”
- Wavelength (frequency) Range: 100 nm -1 mm (3000 THz – 300 GHz)
- Exposure Duration: 10 femtosecond – several hours (“long duration” exposure)
- Irradiance Diameter: micrometers (retinal focal exposures) – meters (whole body)
- Repetitive pulse exposures (e.g., nanosecond pulses at a 10,000 pps rate)
- Repeated exposures separated by minutes, hours or days

Data Gap: Optical Radiation – Protective Exposure Limits

Optical Radiation Exposure Limits (ELs) based upon a robust Data Set

- Dose-response relationships for a range of exposure conditions
- Exposure models include:
 - Animal Models (eye and skin)
 - Cellular Models
 - Computational Models (e.g. thermal model) anchored to adverse biological effects thresholds and extend the data set to uninvestigated exposure conditions
 - Human exposure assessments
 - Epidemiology
- Biological Endpoints
 - Clinical (e.g., direct observation to advanced imaging) criteria, subcellular effects (e.g., microscopic, proteomic changes) to temporary or permanent changes in function of the organism (e.g., vision)
 - Mechanism understanding (e.g. photochemical, photothermal, microcavitation, et cet.)

Data Gap: Optical Radiation - Exposure Limits

Exposure Limits (ELs) for Optical Radiation

- Cover a wide range of exposure conditions
- Protect against adverse effects without being too restrictive
- ELs are algebraically complex
- Compliance measurements are difficult

New Applications of Optical Radiation Change Potential Exposure

- Advanced imaging (e.g. wavefront-corrected, high resolution retina imaging, or endoscopic OCT (optical coherence tomography))
- Active multispectral surveillance and imaging systems
- Emissions from new displays or systems where active near-infrared is used for gesture recognition and system control
- Advanced or new luminaires (PC LEDs) for home and office

New research to assure Exposure Limits are protective needs to be identified and supported. The ICNIRP “Data Gap Project”

Data Gap: Optical Radiation - Research Areas (1)

Photochemical Retinal Effects from Long Duration Exposures

- Retinal biological effects data for exposures >100 seconds
- Recent reports of the disruption of primate retinal pigment epithelium by fluorescence adaptive optics scanning laser ophthalmoscopy for yellow and **infrared** light for long exposure durations at doses near or below current retinal thermal limits.
- **Human volunteers: no effect on vision**
- Research important to advance retinal imaging systems and possible long term effects of light exposure

Afterimages Perceived after Short Duration Visible Light Exposure

- Persistent grey afterimages observed in human exposure after short (0.25 s), blue light exposure research near the retinal thermal exposure limit
- No known retinal injury – possible unexpected photochemical effect

Chronic Light Exposure and Age Related Macular Degeneration (AMD)

- Both biological and epidemiological research needed to understand the implication of chronic light exposure to retinal aging

Data Gap Project: Optical Radiation - Research Areas (2)

Additive Effects of Repetitive Pulse and Repeated Exposures

- Additional research needed to adjust ELs for repetitive pulse exposure as function of wavelength, pulse duration, pulse repetition rate, pulse train duration, and irradiance diameter for **retina, iris and lens**.
- Biological effects and computation models to understand mechanisms and **adjust** ELs

Neuroendocrine Effects of Light

- Blue light exposure of the retina alters the circadian system, suppresses release of melatonin, and disrupts sleep cycles
- Additional research needed to understand the mechanisms, effective dose and possible need for new ELs and/or guidance
- Implication to new phosphor converted LED luminaires for home and office