To the Office of the Assistant Secretary for Health:

I am a member of the public submitting comments in response to the Request for Information on Electromagnetic Fields (EMFs), Radiofrequency (RF) Radiation, and Wireless Radiation Exposure published September 21, 2026 (Docket HHS-OASH-2026-0397). My comments address one specific question in the RFI: how to convert the current, largely unresolved debate over non-thermal effects of RF/EMF into a research program capable of distinguishing established evidence from emerging findings and areas of uncertainty.

My core recommendation is that HHS should fund research using a blinded, quantitative molecular endpoint panel — human endogenous retrovirus (HERV) transcription, calcium-signaling readouts, and interferon/dsRNA markers — applied both in vitro and directly in human studies. These endpoints are already validated in adjacent fields (virology, immunology, oncology), require no novel technology, and are machine-read rather than observer-read, which directly addresses the reproducibility failures that the RFI itself identifies in the existing RF/EMF literature.

Background and Scientific Rationale

The RFI asks respondents to distinguish established evidence, emerging findings, and uncertainty. The current state of the proposed mechanism chain is:

1. **Established**: HERVs constitute ~8% of the human genome and are epigenetically silenced (DNA methylation, H3K9me3, KRAB-ZFP/TRIM28). This is textbook-level established science.
2. **Emerging**: HERV reactivation (notably HERV-K HML-2 and HERV-W loci) is driven by calcium-dependent transcription factors (NF-AT, NF-κB), oxidative stress, and interferon feedback loops, and is implicated in multiple sclerosis, ALS, and autoimmune conditions. Multiple independent groups have validated locus-specific measurement methods in peripheral blood.
3. **Uncertainty**: Whether non-thermal RF/EMF exposure can initiate this chain via voltage-gated calcium channel (VGCC) activation. Pall's VGCC hypothesis and the ROS/NOS oxidative-stress literature remain contested. A 2024 systematic review (Henschenmacher et al., *Environment International* 2024) rated the evidence linking RF-EMF to oxidative stress as very low certainty — chiefly because of high risk of bias (unblinded designs, poor exposure assessment) rather than because of consistent negative findings.
4. **Near-empty**: Direct evidence linking RF/EMF exposure to HERV transcription is essentially absent. To my knowledge only a single exploratory study (ELF-EMF in melanoma cells) exists. By contrast, ionizing radiation is a well-characterized HERV reactivator (ATM–KAP1 pathway), which establishes the plausibility of the downstream biology while leaving the non-ionizing trigger untested.

This is precisely the situation the RFI describes as an area of uncertainty that warrants targeted study: a plausible but untested mechanism, existing validated tools, and a literature whose quality problems are methodological and therefore fixable.

Core Recommendation: A Three-Track Human Research Program

Rather than adding another generation of unblinded in vitro studies, I recommend that any HHS-funded program prioritize human studies using a common molecular endpoint panel. The three-track design below, combined with end-to-end blinding, cell-composition correction, and pre-registered analysis pipelines, constitutes the most actionable contribution of this comment.

Common molecular endpoint panel

- **HERV transcription**: locus-specific qRT-PCR for validated sentinel loci (e.g., HERV-K102, HML-2 22q11.23, HERV-W env), with RNA-seq confirmation in a subset.
- **Calcium-signaling readouts**: in human studies, proxy readouts are limited; the panel should therefore include NF-AT–regulated gene expression and calcineurin pathway markers in PBMCs, acknowledging this as the weakest link (see limitations below).
- **Interferon/dsRNA markers**: IFN-α/β, interferon-stimulated genes (e.g., ISG15, MX1, OAS1), and cytokine panels (IL-1β, IL-6, TNF-α).

Track 1 — Double-blind provocation study.

Participants undergo active and sham RF exposure in a shielded room, randomized and counterbalanced, with blood draws at baseline, 4 h, 24 h, and 72 h. Prior provocation studies (~30 double-blind studies exist) tested symptoms and cortisol but never HERV or interferon endpoints. **Blinding must extend to exposure-chamber operators, laboratory staff, and bioinformaticians; analysis pipelines should be pre-registered.**

Track 2 — Occupational cohort with personal dosimetry.

Telecommunications tower workers, radar operators, and broadcast engineers, matched controls, wearing personal exposimeters for 1–2 weeks with repeated blood sampling. This track delivers the dose–response data that the RFI identifies as a critical gap, and simultaneously builds the personal exposure assessment capacity (including 5G mid-band and mmWave) that HHS and NIST have separately flagged.

Track 3 — Natural experiment / self-controlled design.

Longitudinal sampling of residents before and after base-station activation, deactivation, or frequency upgrade, using each participant as their own baseline. HERV expression varies enormously between individuals; self-controlled designs eliminate most of this variance and require no control group recruitment.

Methodological Requirements

To avoid repeating the quality failures of the existing literature, HHS should make the following conditions of funding. **The four items highlighted below are the highest-priority, most actionable requirements.**

1. **End-to-end blinding**: sample coding before assay, blinded laboratory and bioinformatics analysis, pre-registered analysis pipelines.
2. **Cell-composition correction**: HERV transcription in peripheral blood is highly cell-type-specific and largely granulocyte-attributed; whole-blood measurements without CBC/flow cytometric correction will produce spurious findings.
3. Multi-timepoint sampling: HERV transcriptional responses are transient (peaking ~24 h and normalizing by ~72 h in analogous radiation studies); single-timepoint designs risk false negatives.
4. Chamber engineering controls: continuous temperature logging, sham-exposure chamber verified for RF cleanliness, and cross-over of exposure chambers between arms.
5. Pre-specified sentinel loci: to avoid the well-known multi-mapping problem of repetitive-element quantification, primary endpoints should be restricted to loci with validated, independently reproduced assays (HERV-K102 and a small set of HML-2/HERV-W loci), with genome-wide analysis as secondary/exploratory.
6. Symptom and molecular endpoints reported separately: double-blind studies have consistently shown that self-reported symptoms do not track actual exposure; molecular endpoints must not be validated against, or discounted by, subjective report.
7. Replication by design: each in vitro finding must pass a second laboratory with independent exposure infrastructure before being cited as evidence.

Honest Statement of Limitations

I want to state clearly what this proposal does not claim:

- It does not claim that RF/EMF exposure activates HERVs; that question is precisely what the proposed research would test.
- It does not claim that a positive molecular finding would constitute evidence of harm. HERV activation is a cellular stress signature, not a health outcome. The value of these endpoints is mechanistic resolution, not risk assessment by itself.
- The calcium-signaling link is the weakest portion of the chain in human studies: in vivo calcium dynamics in deep tissues cannot be imaged, and PBMC proxy readouts (NF-AT/calcineurin) are an imperfect substitute. In vitro calcium imaging must therefore remain part of the program as the bridge between tracks.
- If all three marker classes are consistently negative under rigorous blinded conditions, that result should be published and treated as narrowing the uncertainty — not as a failure of the research program. A research design that cannot fail is not a research design.

Specific Asks

I respectfully request that HHS:

1. Include HERV transcription (sentinel-locus qRT-PCR) and interferon/dsRNA markers among the molecular endpoints recommended for federally funded RF/EMF research;
2. Prioritize human studies (blinded provocation, occupational dosimetry cohorts, natural experiments) over further unblinded in vitro work, while requiring the methodological conditions listed above (especially end-to-end blinding, cell-composition correction, and pre-registered pipelines);
3. Fund a standing biorepository of coded blood samples from these studies so that future endpoint discoveries can be tested retrospectively without new exposure;
4. Coordinate with the NIST/NIBIB medical metrology roadmap (Docket NIST-2026-0133) to ensure personal exposimetry across 5G bands is standardized in parallel with the biology;
5. Ensure that the distinction between established evidence, emerging findings, and uncertainty is applied explicitly to each published result — including negative results.

Research Design Outline

B1. Common Molecular Endpoint Panel

Endpoint	Assay	In vitro	Human	Tier
HERV-K102 expression	locus-specific qRT-PCR	✓	✓	Primary
HML-2 22q11.23 and other sentinel loci	locus-specific qRT-PCR	✓	✓	Primary
HERV-W env	qRT-PCR (validated primer sets)	✓	✓	Primary
Whole HERV transcriptome	RNA-seq + Telescope or equivalent pre-registered pipeline	✓	subset	Exploratory
Intracellular Ca^{2+}	fluorescent calcium imaging (Fluo-4 etc.)	✓	—	Mechanistic bridge

NF-AT / calcineurin activity	NF-AT nuclear translocation / reporter; dephosphorylation assays	✓	PBMC proxy	Secondary
dsRNA / MDA5-MAVS signaling	immunoblot / ISRE reporter	✓	—	Exploratory
IFN-α/β, ISGs (ISG15, MX1, OAS1)	ELISA + qPCR	✓	✓	Primary
Cytokines IL-1β, IL-6, TNF-α	multiplex bead assay	✓	✓	Secondary
Oxidative stress (8-OHdG, GSH/GSSG)	ELISA / colorimetric	✓	✓	Secondary
Blood cell composition correction	CBC + flow cytometry	—	✓	Mandatory

B2. Track 1: Double-Blind Provocation Study

- Design: randomized, double-blind, sham-controlled, crossover (within-subject)
- Participants: n ≈ 60–80, including self-reported sensitive individuals and general population (analyzed separately)
- Exposure: controlled RF in a shielded room (bands and SAR per pre-registered protocol; include 5G mid-band); sham chamber verified for RF cleanliness
- Timeline: baseline → single exposure → blood at 4 h / 24 h / 72 h; ≥2-week washout between arms
- Monitoring: continuous chamber temperature logging; participants and operators fully blinded
- Analysis: pre-registered pipeline; samples coded before assay; primary analysis = paired comparison of active vs. sham
- Expected output: clear positive or negative causal conclusion on the molecular endpoints

B3. Track 2: Occupational Cohort

- Design: prospective cohort, high-exposure group (tower maintenance, radar, broadcast) vs. age/sex-matched controls
- Scale: n ≈ 150 per group minimum
- Exposure assessment: personal RF exposimeters worn continuously for 1–2 weeks × 3 waves; fixed-point environmental measurements
- Sampling: one blood draw per wave; simultaneous CBC/flow cytometry
- Analysis: dose–response models treating exposure as continuous; adjustment for cell composition, age, smoking, BMI, infection history

- Expected output: real-world dose–response data and exposure-assessment capacity building

B4. Track 3: Natural Experiment

- Design: before–after longitudinal sampling; each participant serves as own baseline
- Event: base-station activation / deactivation / frequency upgrade (community identified via public siting data)
- Timeline: 4–8 weeks pre-event, then 2 weeks / 3 months / 6 months post-event
- Scale: n ≈ 100–200 residents
- Strength: eliminates most inter-individual HERV expression variance; low cost and scalable
- Limitation: non-randomized; must adjust for seasonal, infection, and stress confounds

B5. Quality Gates (common to all tracks)

1. Pre-registration of protocol, endpoints, analysis pipelines, and exclusion criteria in a public repository (e.g., OSF)
2. End-to-end blinding; analysts see only sample codes
3. Equal publication obligation for negative and positive results
4. Cross-tool sensitivity analysis (≥2 independent HERV quantification pipelines)
5. Mycoplasma / microbial contamination screening (in vitro); acute infection exclusion (human)
6. Temperature-field and sham-chamber verification reports published with the paper

B6. Interpreting Results Against the RFI's Taxonomy

Finding	Classification
All three marker classes change, replicate across laboratories, and show consistent dose–response	**Emerging finding (downstream health significance still unestablished)**
Effect seen in only one laboratory or one track	**Area of uncertainty → drives further exposure standardization**
Consistently negative under rigorous blinding	**Narrows the uncertainty range → this specific pathway (VGCC → HERV → IFN) is downgraded**

Calcium changes but HERV/IFN do not	**Distinguishes “calcium sensitivity (partially supported)” from “presumed downstream cascade (unsupported)”**

Selected References

1. Henschenmacher B, et al. The effects of radiofrequency electromagnetic field exposure on biomarkers of oxidative stress in vivo and in vitro: A systematic review of experimental studies. *Environ Int.* 2024;194:108940. doi:10.1016/j.envint.2024.108940
2. Geisler C, et al. Activation of human endogenous retroviruses and its physiological consequences. *Nat Rev Mol Cell Biol.* 2024;25:212-222.
3. Del Re B, et al. Effect of electromagnetic field exposure on the transcription of repetitive DNA elements in human cells. *Electromagn Biol Med.* 2019;38(4):262-270.
4. Afsordeh K, et al. Effects of prolonged exposure to ELF-EMF on HERVs expression in human melanoma cells. *Electromagn Biol Med.* 2022. PMC9336785.
5. Grandi N, Tramontano E. Human endogenous retroviruses and cancer: a comprehensive review. *Front Microbiol.* 2018.
6. Perron H, et al. Human endogenous retrovirus and multiple sclerosis. *Curr Opin Neurol.* 2017.
7. Pall ML. Electromagnetic fields act via activation of voltage-gated calcium channels to produce beneficial or adverse effects. *J Cell Mol Med.* 2013;17(8):958-965. (Note: hypothesis remains contested.)
8. Wang X, et al. Ionizing radiation induces HERV reactivation via ATM–KAP1 pathway. Relevant literature on radiation and endogenous retrovirus reactivation.
9. Multiple independent validations of locus-specific HERV-K and HERV-W qRT-PCR assays in peripheral blood (representative methods papers available upon request).

End of comment.

This submission focuses exclusively on converting an area of genuine scientific uncertainty into a falsifiable, methodologically rigorous research program.