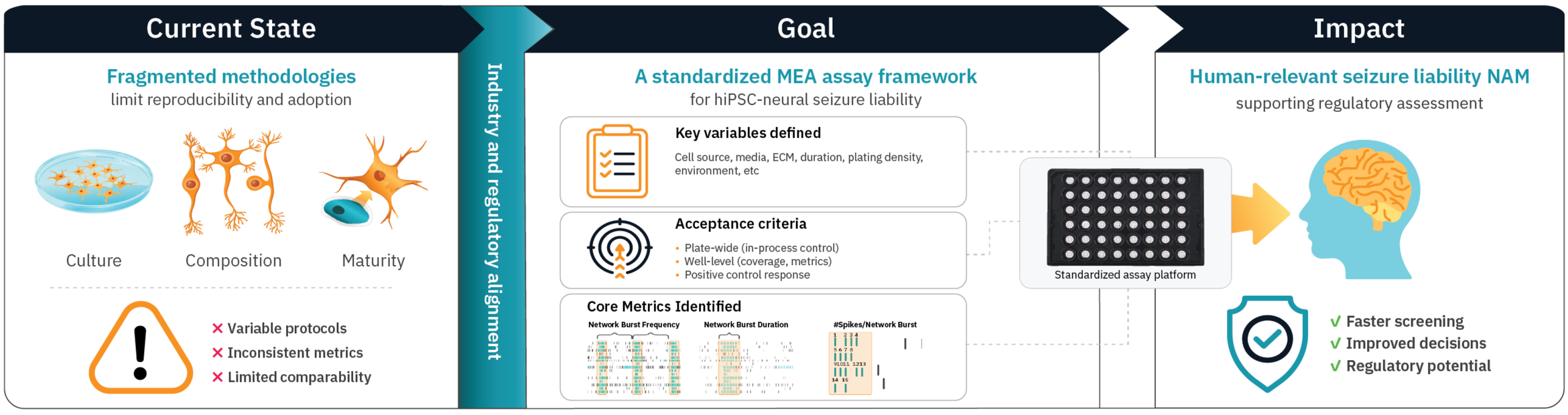
# >> Establishing Functional Acceptance Criteria for hiPSC-Neural MEA Seizure Liability Assays

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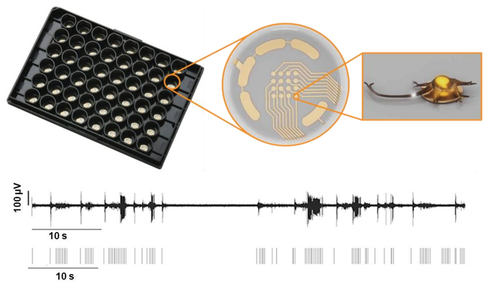

**Key Takeaway:** The proposed functional standard is to improve reproducibility and cross-laboratory consistency in hiPSC-neural seizure liability MEA assays

## Methods

This project establishes a functional framework for hiPSC-neural seizure liability MEA assays through published evidence and expert input.

- **Review of 11 published studies**
- **Input from 11 experienced laboratories**
- **Consensus-derived framework**

### MEA Platform




Multiwell MEA plate (CytoView MEA 48-well plate, *left*) with a 4x4 grid of 16 recording electrodes in the base of each well (*middle*). The MEA electrodes are sensitive enough to detect the activity of individual neurons (illustration not to scale, *right*). Spontaneous neural field potential recording from one MEA electrode (*top trace*) and corresponding raster plot (*bottom trace*).

## Key Variables Defined

**Which factors influence network activity?**

### Cell Culture
- Cell composition
- Density & distribution
- Days *in vitro*

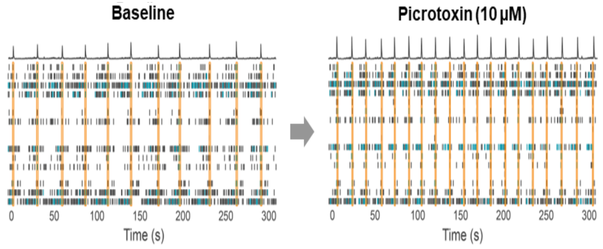
### Environmental
- Temperature
- $CO_2$
- Culture Media & Feeding

### Assay
- Recording Time
- Dose Method
- Replicates

Standardizing these variables reduces variability and improves assay comparability.

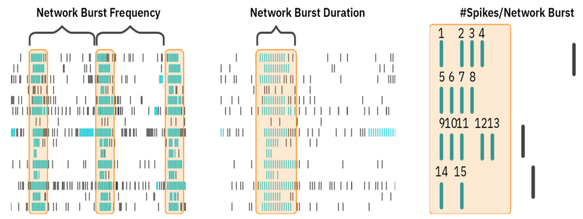
## Core Metrics Identified

**What does seizurogenic activity look like in the MEA assay?**




Raster plot from hiPSC-neuronal cells in a well of a CytoView 48-well MEA plate (16 electrodes per well), recorded on Day 23 before and after exposure to picrotoxin (PTX).

### Metrics




Seizurogenic compounds typically increase one or more parameters of network burst activity, including network burst frequency (NBF), network burst duration (NBD), and the number of spikes per network burst (#spikes/NB).

## Acceptance Criteria

**What should baseline activity look like for a culture to be used in the MEA assay?**

**Plate-level acceptance:**

≥80% of wells meet all baseline acceptance criteria

**Well-level acceptance:**

| Metric | Proposed Threshold |
|---|---|
| Active electrodes | ≥10/well (16-electrode format)<br>≥6/well (8-electrode format) |
| Network burst participation | ≥40% active electrodes |
| Network burst frequency | ≥0.013 Hz |
| Synchrony index | ≥0.15 and ≤0.85 |

**Positive control response:**

PTX (10 µM) produces ≥25% increase in at least one: NBF, NBD, and/or #spikes/NB

## Conclusion

This work establishes a pragmatic, evidence-based framework for standardizing hiPSC-neural seizure liability MEA assays. By defining baseline activity thresholds, positive control responses, and recommended reporting practices, the proposed functional standard supports improved reproducibility, cross-study comparison, and broader adoption of the assay as a human-relevant NAM in safety pharmacology.

## Why it matters

- Enables cross-lab consistency
- Supports safer and more efficient drug development
- Advances regulatory science and NAMs

## Learn more

Scan the QR code to visit our website to access a copy of the full paper

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