

## Clinical Trial Registration PRS Cover Page

**Document:**

Protocol

**Official Title:**

Personalized Mobile Intervention to Reduce Exposure to Endocrine Disrupting Chemicals (EDCs) in Women of Child-Bearing Age and Their Partners

**NCT Number:**

NCT05780047

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**Title of Study:** Renown Institute for Health Innovation-Million Marker Detect and Detox Pilot

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## **Study Purpose and Narrative**

1. *Describe the study background, significance, and purpose/hypothesis/research questions.*

The exposome encompasses all of the environmental exposures across one's lifespan<sup>1</sup> and includes toxic chemical exposures from food, water, air, and household and consumer products.<sup>2</sup> It is the exposome *and* the genome that determines our health.<sup>1</sup> And in fact, environmental factors are responsible for *more than 70% of the risk* of developing chronic diseases.<sup>3</sup> Thus, assessing the state of the exposome of the population is a crucial factor in assessing public health and advancing recommendations and regulations.

There are over 85,000 man-made chemicals in use today in the U.S., but only 1% have sufficient safety information.<sup>4</sup> Individuals come into contact with these chemicals every day through food and products, such as personal care and household products. Many of these products contain endocrine disrupting chemicals (EDCs). Due to their ubiquitousness, impacts on the environment, wildlife, and human health, EDCs have become a major public health concern.<sup>5</sup> Data from the NHANES has shown that more than 90% of US adults have detectable levels of common EDCs, such as bisphenol A (BPA) and phthalates, in their urine.<sup>6,7</sup> EDC exposures are particularly concerning for reproductive-aged women. Women are the primary consumers of many personal care products,<sup>7</sup> and exposures during pregnancy predispose the fetus to adverse health effects later in life.<sup>4</sup>

Exposure to EDCs across the U.S. population is suspected to cause many chronic diseases and disorders, including IQ loss, intellectual disability, attention-deficit hyperactivity disorder, childhood obesity, adult obesity, Type 2 diabetes, cardiovascular and metabolic disease, genital defects, infertility, and mortality from reduced testosterone.<sup>5,8-10</sup> The economic burden of the diseases caused by all EDC exposure is estimated at \$340 billion in the United States, which is 2.33% of the GDP.<sup>15</sup> In order to mitigate the health impacts and corresponding financial burden of exposures to EDCs, large-scale biomonitoring of populations is crucial for developing Health recommendations and regulations. Further, individuals must have access to an affordable, easy, and rapid way to test their exposures to a wide range of EDCs so that they can reduce their exposures.

Million Marker (MM) is a recent company that offers the first at-home EDC testing kit and environmental exposure journal app. We provide affordable and scalable personalized environmental exposure testing and analysis followed by a tailored intervention program to empower individuals to optimize their health, prevent diseases, and manage existing conditions.

The exposome can be assessed through targeted biomonitoring of exposure biomarkers. Currently, targeted biomonitoring is conducted by the Centers for Disease Control and Prevention (CDC) through the National Health and Nutrition Examination Survey (NHANES).<sup>11</sup> As of 2019, 14 states have established their own biomonitoring programs to monitor chemicals of local concern.<sup>12</sup> These programs provide some baseline data;<sup>13</sup> however, the sample sizes are restricted and no longitudinal data on the same participant is collected.<sup>14</sup> A Million Marker-Renown Institute for Health Innovation (RIHI) collaboration (MM-RIHI) could potentially monitor over 60,000 individuals enrolled in Renown's Healthy Nevada Project (HNP) and provide information such as location, demographic, and lifestyle factors related to the exposome, as well as link the genomic information to the exposomic information of these individuals. These individuals could also be assessed over time to determine longitudinal changes, particularly with interventions in lifestyle changes to reduce exposures. Because the MM kit and app are easy to use, convenient, and non-invasive, a MM-RIHI collaboration could provide ample data with minimal effort and risk.

The HNP is the largest community-based population health study in the world, with more than 60,000 participants. This is twenty times larger than NHANES, the largest nationwide population biomonitoring cohort. It's also the first population health study to return clinical results to study participants.

The collaboration between the Renown Institute for Health Innovation (RIHI) and Million Marker would 1) increase biomarker collection and discovery and 2) increase the exposure assessment database (both internal and external) conducted among existing and future project participants. The HNP Project would be the largest population environmental biomonitoring program in the world, and also the first one to report back the biomonitoring results. As most of Million Marker's current users are between the ages of 25-44, this collaboration may help the HNP recruit younger participants. For Million Marker, this collaboration would allow us to collect large amounts of samples/data to further improve our existing platform, enable AI-assisted exposure assessment and prediction, and drive long-term value for our users including the HNP participants.

To initiate this collaboration, we are proposing a pilot to offer our service to individuals within the participants in the HNP and/or through the Renown Healthcare system.

The aims of this pilot study are:

- 1) Test the feasibility of offering MM's service to the HNP existing and future participants
- 2) Collect pilot data and assess EDC levels among participants
- 3) Test the usability and perception of MM's service among participants
- 4) Test whether offering MM's service can lead to EDC reduction behaviors among participants

- 5) Utilize pilot study data to prepare for larger research studies and grant applications
2. *Provide a detailed narrative, non-technical description of the project and of the planned activity for the participants and/or data collection.*

This project will assess the EDC exposure of participants, through urine testing and self-administered journals. We will recruit up to 300 people (aged 18-40) from the existing participants from the Healthy Nevada Project. Participants' urine samples will be collected via mail-in kits that will be sent to participants. Participants will follow Million Marker's current user journey that involves the following: 1) users receive MM's test kits in the mail, 2) take a comprehensive 24-hour food and product exposure survey via the MM app, 3) collect their first void urine sample in the morning, 4) send back their samples, 5) view their personalized reports with tailored product recommendations through a secure online portal, 6) make changes to reduce their exposures, 7) test again to track/monitor/confirm EDC levels if any behavioral changes have been made.

Participants can make changes to reduce their exposures according to the recommendations in their personalized reports. Participants will receive a second test kit three weeks after getting their initial reports, and be asked to complete and ship it back within one week after receiving it in the mail. All participants will be offered the second test kits as there will always be room for chemical reduction.

Participants will fill out the System Usability Scale (SUS) to evaluate the usability of the Million Marker app and their experiences (engagement, satisfaction, and retention) upon the receipt of their reports for both rounds of testing.

## **References:**

1. Wild, C. P. Complementing the genome with an 'exposome': the outstanding challenge of environmental exposure measurement in molecular epidemiology. *Cancer Epidemiol Biomark. Prev* **14**, 1847–50 (2005).
2. Wild, C. P. The exposome: from concept to utility. *Int J Epidemiol* **41**, 24–32 (2012).
3. Rappaport, S. M. & Smith, M. T. Environment and Disease Risks. *Science* **330**, 460–461 (2010).
4. Kelley, A. S. *et al.* Early pregnancy exposure to endocrine disrupting chemical mixtures are associated with inflammatory changes in maternal and neonatal

circulation. *Sci Rep* **9**, 5422 (2019).

5. Trasande, L. *et al.* Burden of disease and costs of exposure to endocrine disrupting chemicals in the European Union: an updated analysis. *Andrology* **4**, 565–72 (2016).
6. CDC. Bisphenol A (BPA) Factsheet. *National Biomonitoring Program*  
[https://www.cdc.gov/biomonitoring/BisphenolA\\_FactSheet.html](https://www.cdc.gov/biomonitoring/BisphenolA_FactSheet.html) (2017).
7. Harley, K. G. *et al.* Reducing Phthalate, Paraben, and Phenol Exposure from Personal Care Products in Adolescent Girls: Findings from the HERMOSA Intervention Study. *Env. Health Perspect* **124**, 1600–1607 (2016).
8. Rochester, J. R. Bisphenol A and human health: a review of the literature. *Reprod Toxicol* **42**, 132–55 (2013).
9. Rochester, J. R., Bolden, A. L. & Kwiatkowski, C. F. Prenatal exposure to bisphenol A and hyperactivity in children: a systematic review and meta-analysis. *Env. Int* **114**, 343–356 (2018).
10. National Academies of Sciences Engineering and Medicine. Phthalates and Male Reproductive-Tract Development. in *Application of Systematic Review Methods in an Overall Strategy for Evaluating Low-Dose Toxicity from Endocrine Active Chemicals* (eds. Division on Earth and Life Studies, Board on Environmental Studies and Toxicology, & Committee on Endocrine-Related Low-Dose Toxicity) (National Academies Press, 2017).
11. CDC. NHANES: National Health and Nutrition Examination Survey.  
<https://www.cdc.gov/nchs/nhanes/index.htm> (2020).
12. CDC. State Biomonitoring Programs. *National Biomonitoring Program*  
[https://www.cdc.gov/biomonitoring/state\\_grants.html](https://www.cdc.gov/biomonitoring/state_grants.html) (2019).

13. CDC. Updated Tables, January 2019. *National Report on Human Exposure to Environmental Chemicals* <https://www.cdc.gov/exposurereport/index.html> (2019).
14. CDC. National Center for Health Statistics National Health and Nutrition Examination Survey Overview.  
[https://www.cdc.gov/nchs/data/nhanes/nhanes\\_13\\_14/NHANES\\_Overview\\_Brochure.pdf](https://www.cdc.gov/nchs/data/nhanes/nhanes_13_14/NHANES_Overview_Brochure.pdf).
15. Attina, T. M. *et al.* Exposure to endocrine-disrupting chemicals in the USA: a population-based disease burden and cost analysis. *Lancet Diabetes Endocrinol.* **4**, 996–1003 (2016).