

## Attachment 22.1: Objectives and Background for the Study of Biomarkers of Exposures and Effects in Agriculture (BEEA)

This revision is proposing the continuation of the Study of Biomarkers of Exposures and Effects in Agriculture (BEEA). This **eight**-year effort has two primary objectives. First, to determine the prevalence and study the etiology of monoclonal gammopathy of undetermined significance (MGUS) in a sample of **2,000** cancer-free, male Agricultural Health Study (AHS) pesticide applicators over the age of 50, with well-characterized occupational exposures and lifestyle factors. MGUS has been recently been observed to precede all cases of multiple myeloma in the National Cancer Institute's Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening trial and multiple myeloma has been observed to occur in excess in the AHS cohort. Preliminary observations from the AHS cohort have also shown that MGUS occurs almost twice as frequently as would be expected in a population of the same age and racial distribution in Olmsted County, Minnesota. To achieve this objective, the prevalence of MGUS in the AHS cohort will be compared with the prevalence in two general population-based cohorts (i.e., Olmsted County and NHANES III) with well-characterized MGUS prevalence levels. The associations between MGUS and specific pesticides within the AHS cohort will be examined and it will be determined whether selected biomarkers are associated with excess MGUS and whether these biomarkers are significantly associated with specific pesticides.

Dust will be collected as part of BEEA for the purpose of evaluating exposures in the rural and agricultural environment, such as endotoxins, and pesticides, which have been shown to settle in dust. These exposures in the dust will be linked both to questionnaire data previously collected to evaluate determinants that influence these levels in the home environment, and to various health outcomes. The questionnaire that accompanies the collection of the dust will allow researchers to evaluate these levels in relationship to home characteristics that may influence the levels, and to ensure that the dust being collected is actually from the home where the participant lives. The questionnaire questions and protocol for dust collection are based on previous NCI studies using similar methodologies<sup>1,2</sup>.

The second objective will establish a resource with the remaining biospecimens **and other samples** collected from the participants for the BEEA study that will be used to evaluate the biological plausibility and the mechanism-of-action of associations between pesticides **and other agricultural exposures** and **risk of** cancers observed in earlier AHS studies. Many of these pesticides are non-genotoxic and their mechanism of carcinogenesis has not been determined. The biospecimen resource will include blood, urine, **saliva/buccal cells, and airborne dust and**

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<sup>1</sup> Residential exposure to polychlorinated biphenyls and organochlorine pesticides and risk of childhood leukemia. Ward MH, Colt JS, Metayer C, Gunier RB, Lubin J, Crouse V, Nishioka MG, Reynolds P, Buffler PA. Environ Health Perspect. 2009 Jun;117(6):1007-13.

<sup>2</sup> Household endotoxin levels and the risk of non-Hodgkin lymphoma. Wang J, Cozen W, Thorne PS, Berhane K, Cerhan JR, Hartge P, Ward MH, De Roos AJ, Severson RK, Morton LM, Bernstein L, Linet MS, Colt JS. Cancer Causes Control. 2013 Feb;24(2):357-64.

house dust samples will also be collected from some participants. We will also enroll and collect biospecimens from an additional 200 individuals who have not lived or worked on a farm as an adult or held a job applying pesticides; these participants will serve as controls in future cross-sectional molecular epidemiologic investigations of specific agricultural exposures and intermediate biomarkers related to cancer or other chronic diseases. The controls will be identified from state voter registries in Iowa and North Carolina and will be frequency-matched to BEEA participants on age, race, and state and county of residence.

Among a subset of participants in the BEEA study, we will also conduct an evaluation of the use of smartphone technology to record daily activities (anticipated N=235). The purpose of this effort is to characterize variability in farming activities and to provide insight into the feasibility of using smartphones to collect exposure information for future use in prospective cohort studies. The participants in this effort will be asked to download and use the smartphone app to document their daily farm routine on 30 randomly selected days over a 6-month period.