Qeios

Peer Review

Review of: "IQOS® Cross-Sectional and Cohort US Study Documentation"

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This manuscript presents detailed protocols for two FDA-mandated post-market surveillance studies (cross-sectional and longitudinal) evaluating IQOS® use patterns, transitions, risk perceptions, and selected self-reported health outcomes in U.S. adult consumers. The article is clearly structured, comprehensive in scope, and transparent regarding funding, sponsorship, and regulatory context. The longitudinal design with repeated follow-up waves and the planned use of GEE models and propensity scoring are methodological strengths. The inclusion of transition patterns (e.g., dual use, switching, relapse, cessation treatment use) is particularly relevant for evaluating real-world impact under MRTP conditions.

However, several important methodological and interpretative issues warrant closer consideration:

Selection bias and representativeness

Recruitment primarily from a manufacturer-maintained consumer database raises substantial concerns regarding representativeness. IQOS® users enrolled in such databases may differ systematically from non-registered users in motivation, product satisfaction, health awareness, or loyalty. Although third-party panels are mentioned, more detail is needed on how sampling weights will correct for structural biases.

Industry sponsorship and independence safeguards

While conflicts of interest are clearly disclosed, the manuscript would benefit from an explicit description of data governance safeguards (e.g., independent statistical oversight, pre-registration of analysis plans, third-party auditing, public availability of protocols and analytic code).

Reliance on self-reported outcomes

All exposure and health outcomes are self-reported without biomarker validation. This limits inference regarding actual exposure reduction and health impact. Particularly for cardiovascular and respiratory

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symptom endpoints, objective verification (even in subsamples) would greatly strengthen causal interpretation.

Attrition management

Although weighting and inverse probability methods are planned, projected attrition rates (12–66% from prior studies) are substantial. Sensitivity analyses for missing-not-at-random mechanisms should be prespecified.

Comparative control group limitations

The reference cigarette group is not randomized and may differ in baseline health, motivation to quit, or socioeconomic factors. Propensity scoring helps but cannot eliminate unmeasured confounding.

Public health framing

Statements in the Discussion suggesting "public health benefit" should be more cautiously phrased, as the protocol does not include long-term clinical endpoints, disease incidence, or biomarker validation. The study can assess behavioral transitions and perceptions but cannot independently establish harm reduction.

Overall, this protocol represents an extensive regulatory surveillance effort and may contribute valuable behavioral transition data under MRTP conditions. However, interpretation of findings—particularly regarding harm reduction or public health benefit—must be conservative and clearly separated from exposure-reduction claims derived from prior toxicological or biomarker studies.

Declarations

Potential competing interests: No potential competing interests to declare.