

Modeling Uncertainty and Variability in Longitudinal Aggregate and Cumulative Risks Using A Nested Loop Approach

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Background

- **Simulation models have been identified as the preferred tool for characterizing uncertainty and variability in longitudinal exposures to multiple sources by multiple routes of exposures.**
- **The American Chemistry Council Exposure Technical Implementation Panel contracted a project team led by The LifeLine Group to develop a Comprehensive Chemical Exposure Framework (CCEF).**
- **Final Report for the project *Construction of a Comprehensive Chemical Exposure Framework Using Person Oriented Modeling* completed in June 2003.**

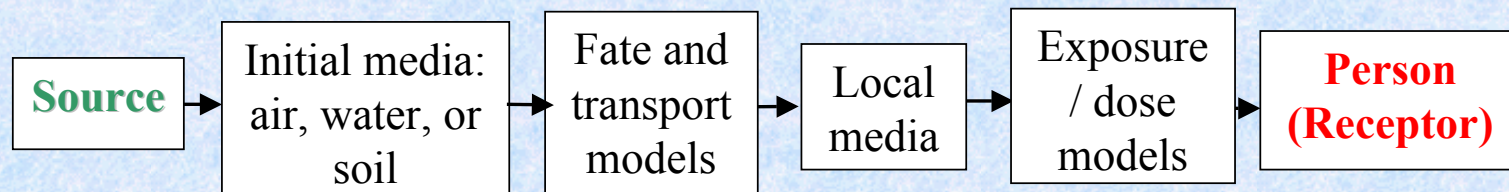
CCEF Must Support

- 1. Exposure by multiple routes;**
- 2. Multiple sources of exposure;**
- 3. Multi-chemical exposure;**
- 4. Variation in a person's exposure over time;**
- 5. Variation across a population; and**
- 6. Uncertainty the model predictions.**

Historical Model Design: Source- to-Dose Models

- Historically the most commonly used model design

Source-to-Dose Models



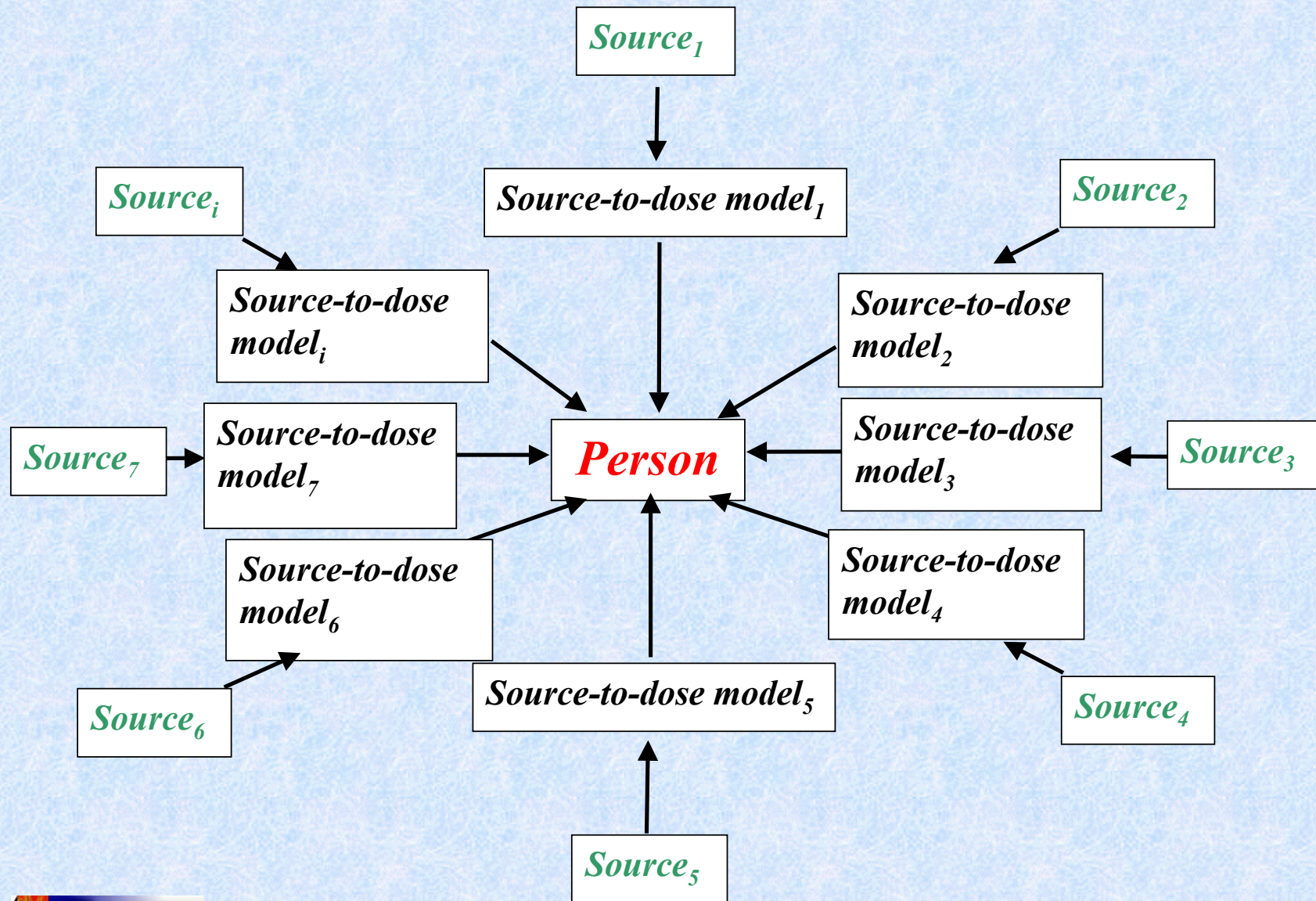
Historical Model Design: Source- to-Dose Models

- Historically the most commonly used model design
- Source-to-dose models offer two advantages
 - They define the relationship between a specific source and the resulting doses in the affected population and
 - Following a chemical from a source to a final dose forces the assessor to systematically address all relevant processes

Problems with Source-to-Dose Models

- Exposure model is defined by the source of the exposure.
 - This causes problems for models of exposures from multiple independent sources of exposure.

Multi-Source Exposure Models



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- The natural result of multi-source models is the placement of the person at the center of the model not the sources.

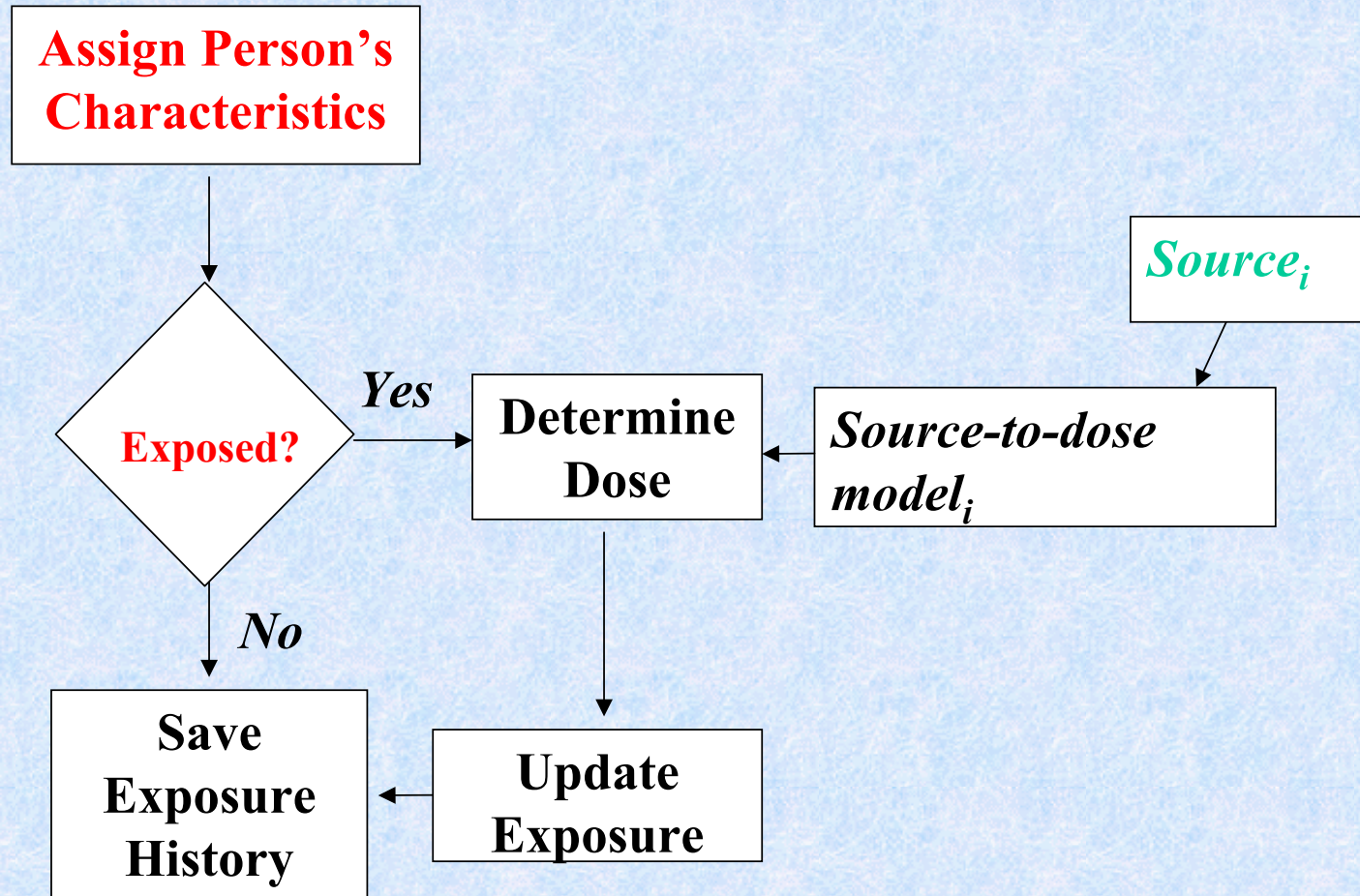
Problems with Source-to-Dose Models

- Exposure model is defined by the source of the exposure.
 - This causes problems for models of exposures from multiple independent sources of exposure.
- The natural result of multi-source models is the placement of the person at the center of the model not the sources.
- The sources are now defined in terms of the person's interaction with the sources.

Person Oriented Modeling (POM)

- POMs begin the modeling process by defining the exposure-related characteristics of the persons in the population

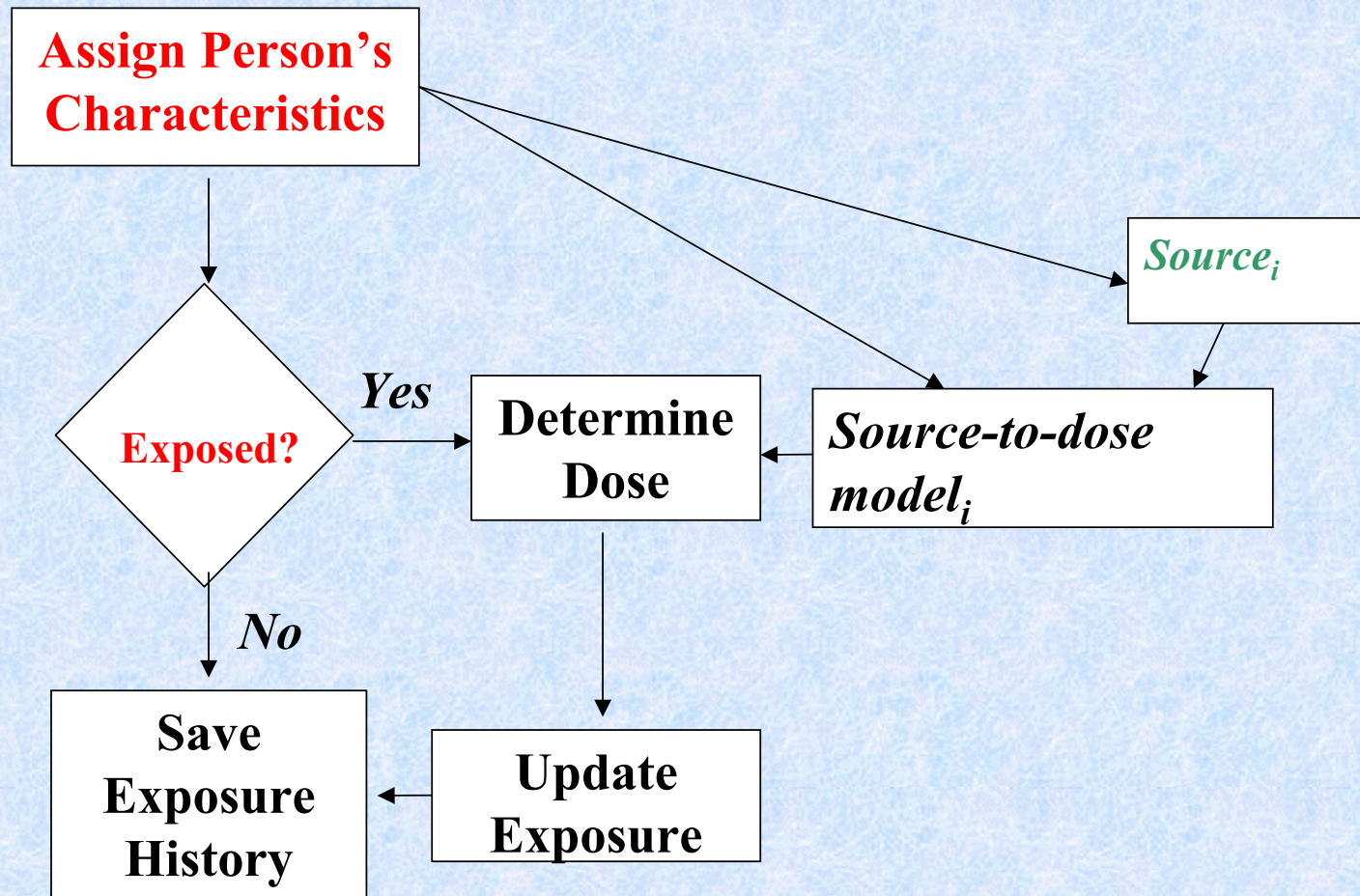
Person Oriented Modeling



Person Oriented Modeling

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- Once the relevant characteristics are defined, they are used to determine the probability of being exposed to a specific source on a given day and, if exposed, the resulting doses.

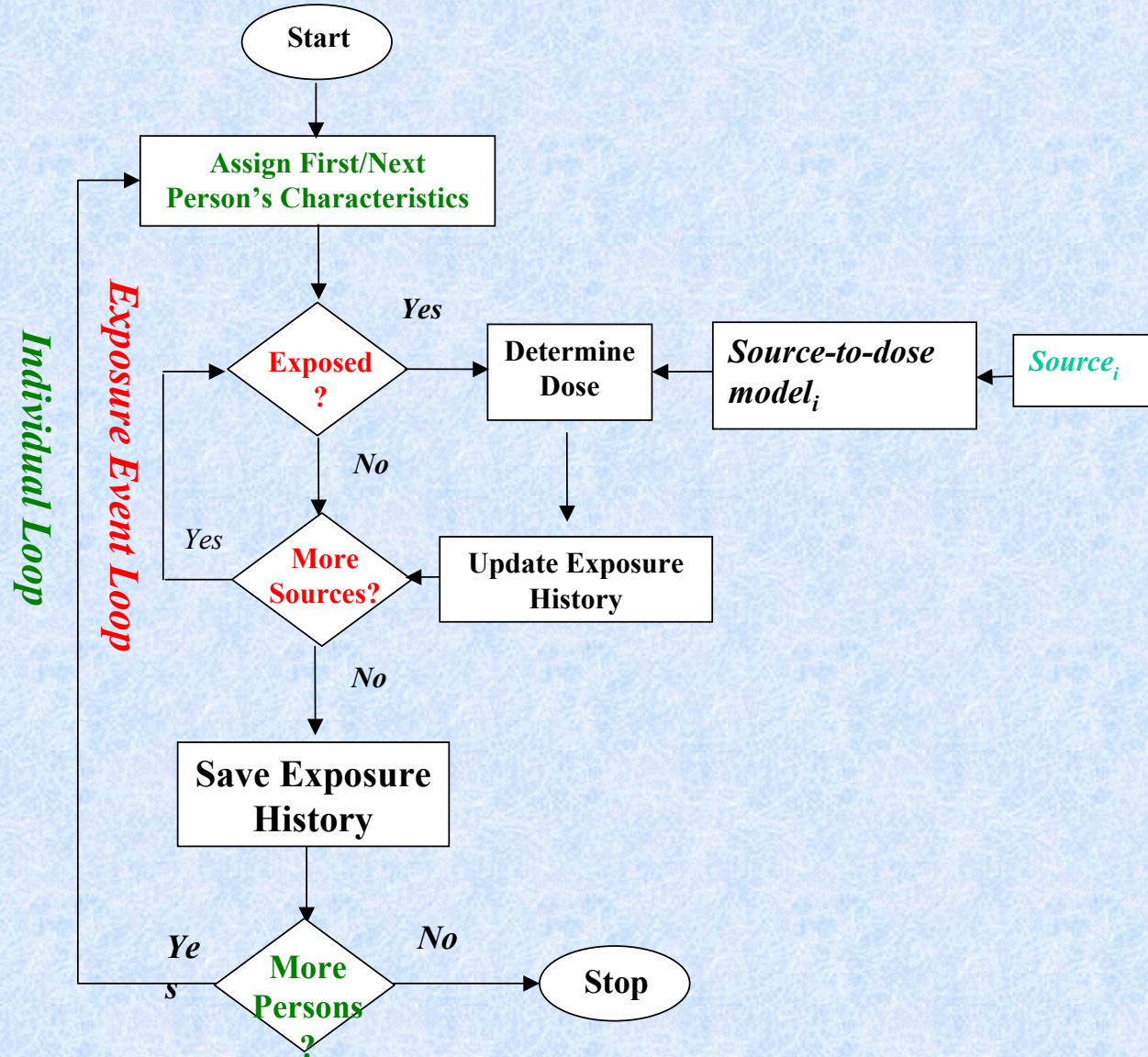
Person Oriented Modeling



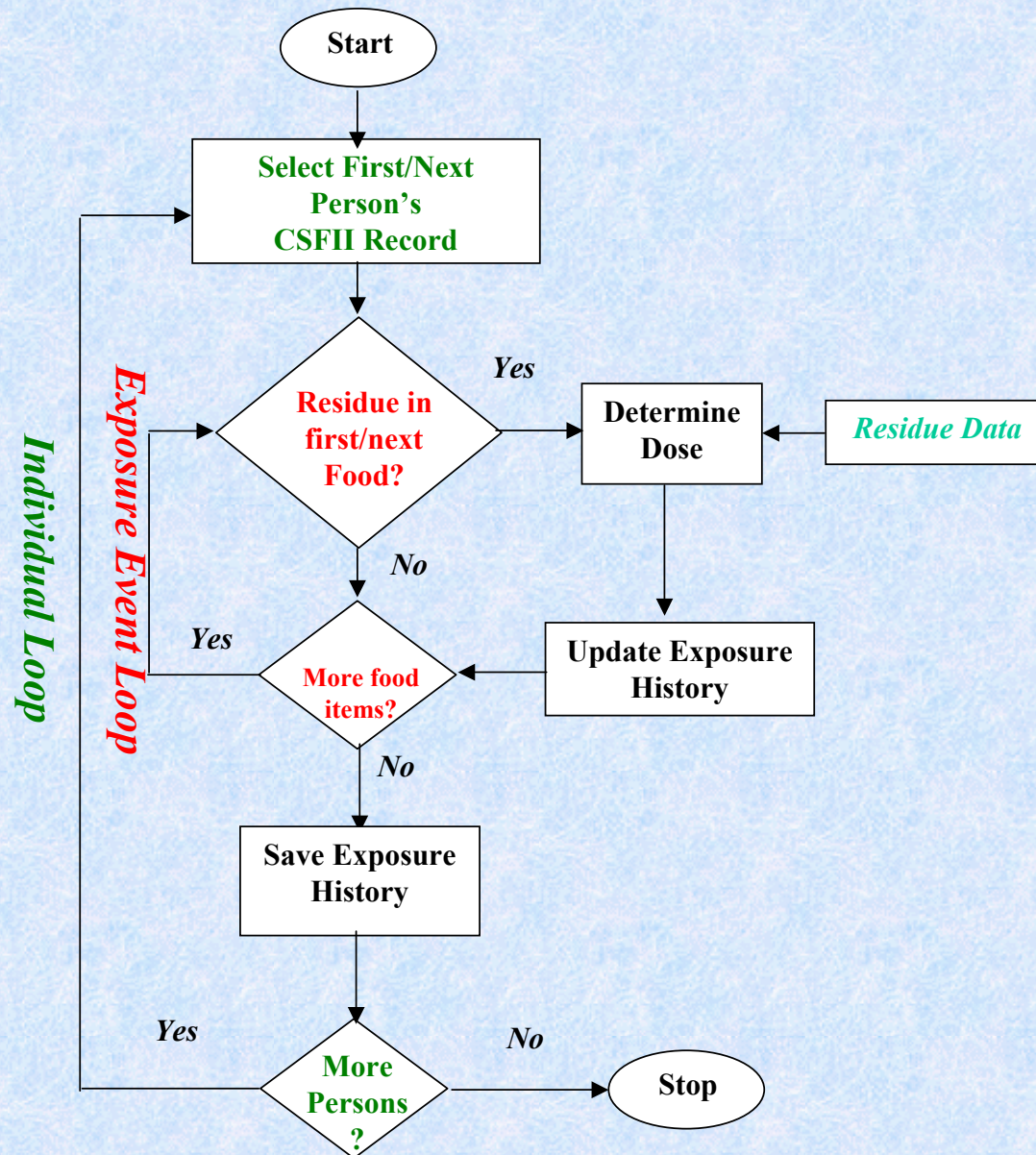
Person Oriented Modeling

- POMs begin the modeling process by defining the exposure-related characteristics of the persons in the population
- Once the relevant characteristics are defined, they are used to determine the probability of being exposed to a specific source on a given day and, if exposed, the resulting doses.
- Thus, while exposure-to-dose models use the source to define the model structure, POMs use the nature of the population to define the model structure.

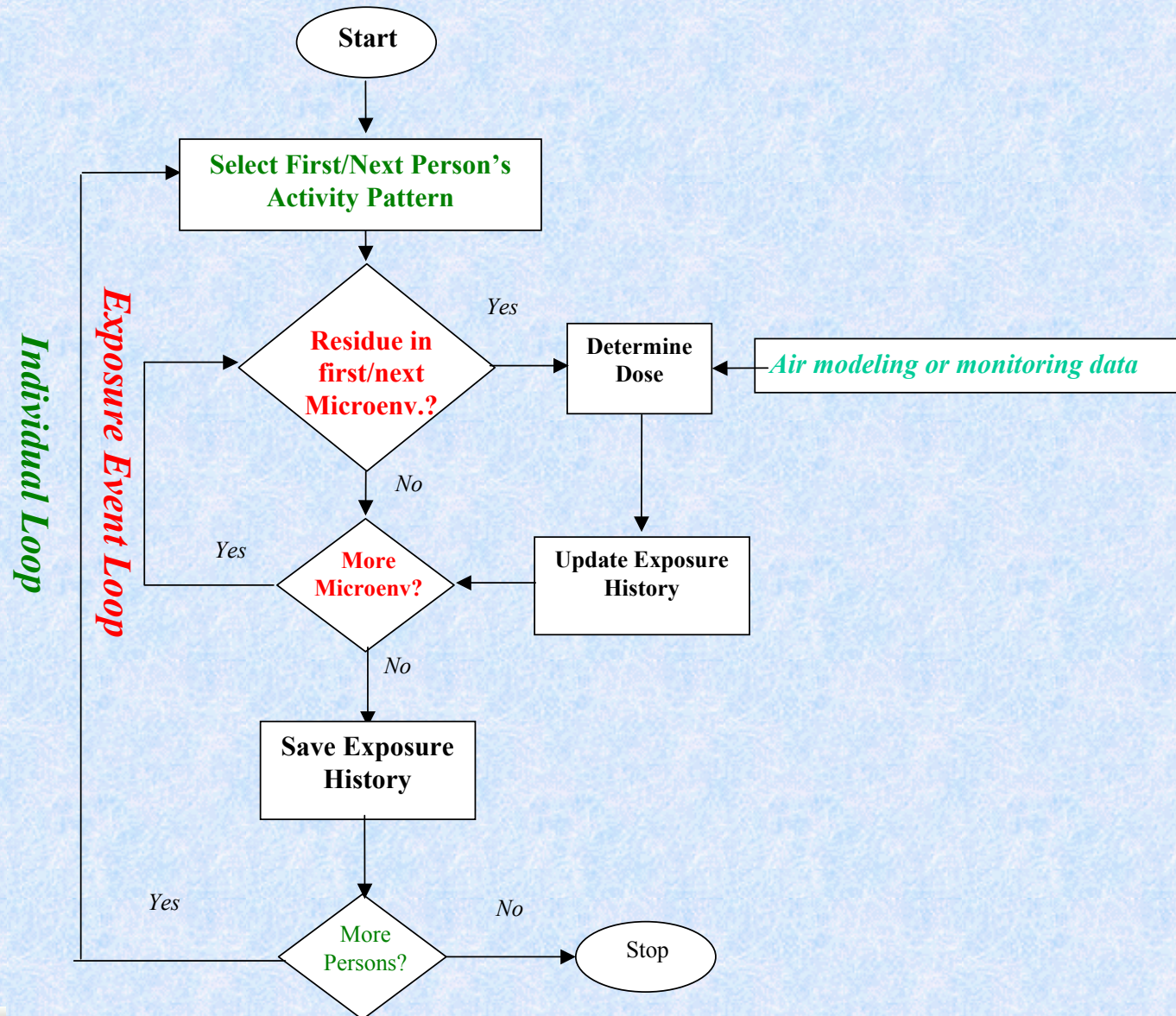
Person Oriented Modeling: Exposure to Multiple Sources



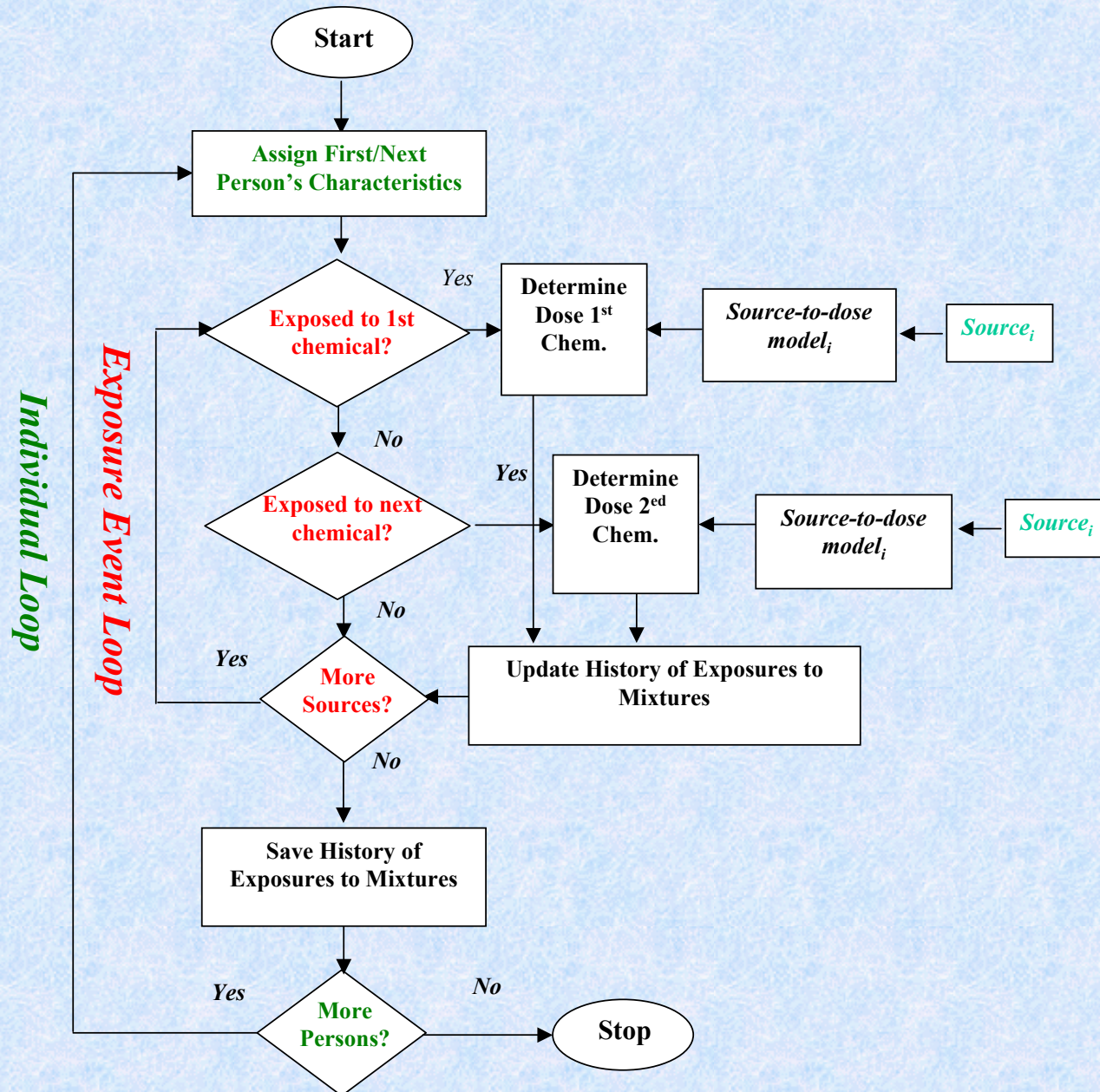
Example of POM: Models of Dietary Exposures to Pesticides



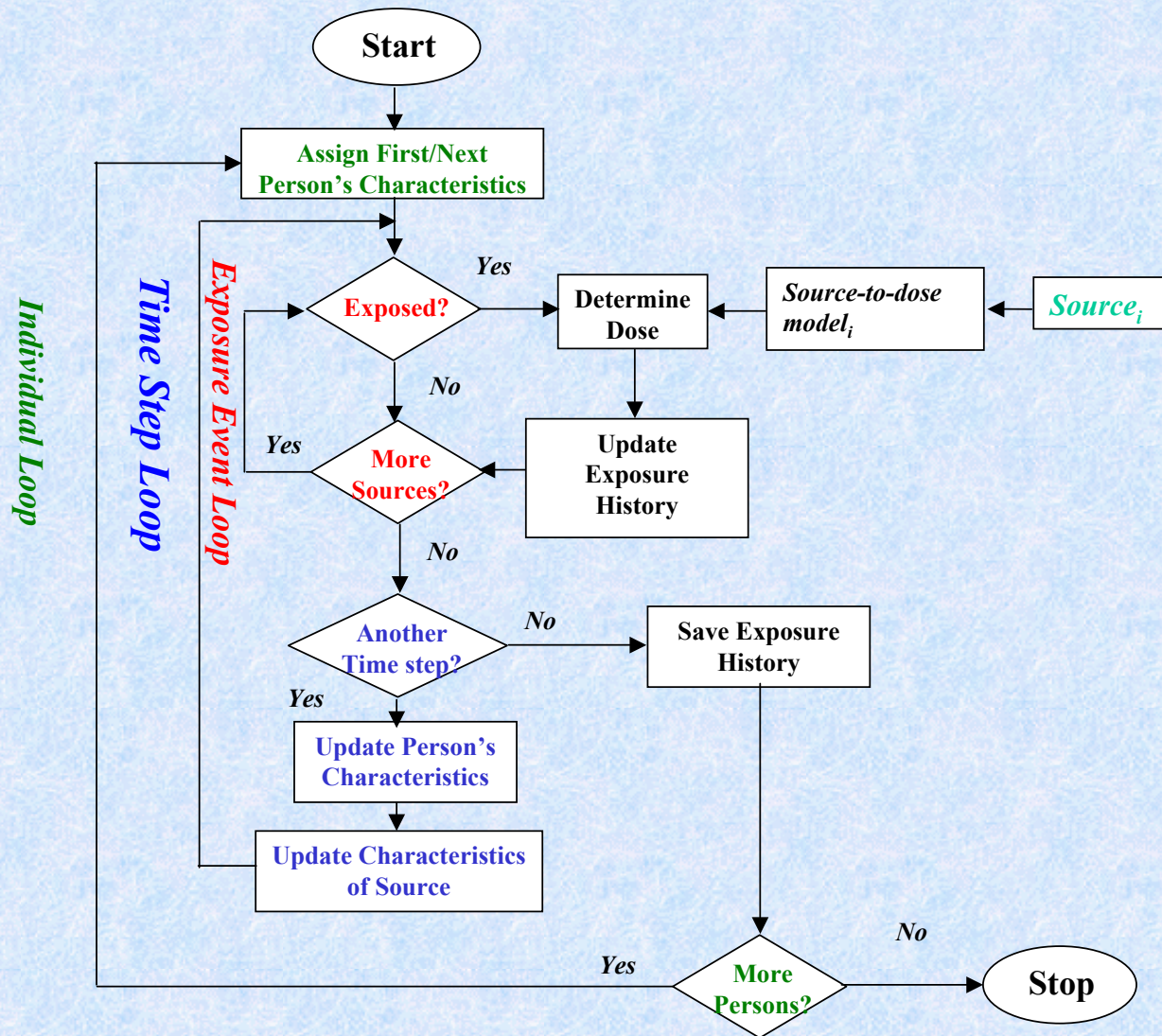
Example of POM: Microexposure Models



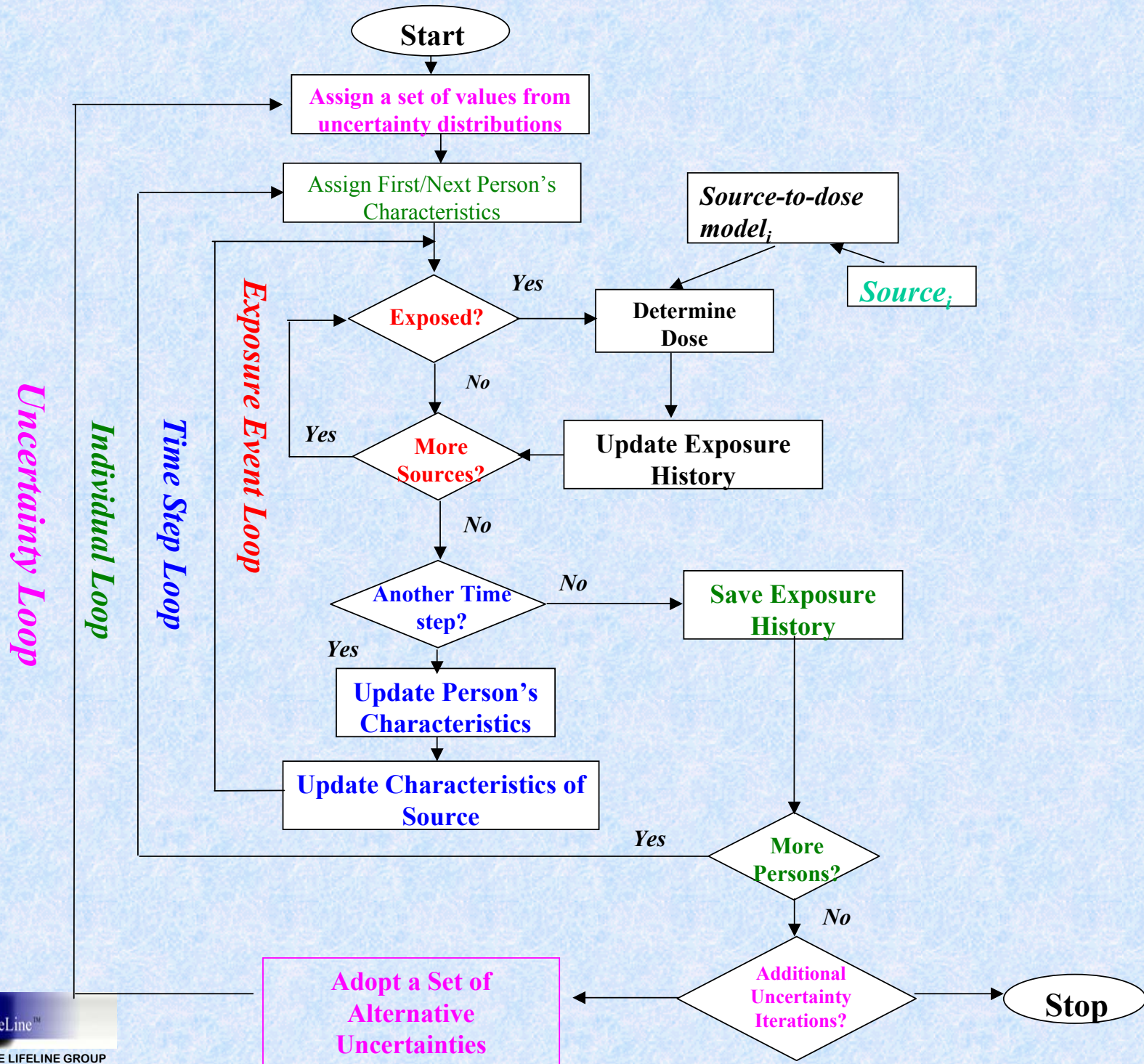
Modeling Exposures to Multiple Chemicals



Modeling Longitudinal Exposures



Final Comprehensive Chemical Exposure Framework



Not a New Idea

- Microexposure models BEAM, SHAPE, and APEX are POMs.
- Aggregate models developed for FQPA, CARES™, LifeLine™, and SHEDS are POMs.

Summary

- The proposed approach, while simple, has the ability to model:
 - Doses from acute to lifetime doses,
 - For ages varying from conception through birth to any age.
- The approach can be extended to:
 - Any number of chemicals,
 - Sources of exposure, and
 - Routes of exposure.
- The approach allows for the correct separation inter- and intra-individual variation and uncertainty.
- Finally, the proposed approach is consistent with many models currently in use or under development by EPA, academia, and industry.

Final Report Is Available

www.thelifelinegroup.org

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