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## Protection of Participants in Research Studies

### COMMON QUESTIONS

- When is it appropriate for surrogate decision-makers to enroll a person with dementia in a research study?
- What is the appropriate risk-to-benefit ratio to consider when deciding to enroll a person with dementia in a research study?
- What principles should guide the decisions of a surrogate?

### BACKGROUND INFORMATION

The Alzheimer's Association® believes that research to prevent, delay onset or slow the progression of dementia is among the most pressing medical imperatives today. The Association also believes that the protection of individuals who participate in such research is essential. Informed consent is a central means of protecting participants while allowing them to exercise self-determination. However, it is impossible to obtain valid informed consent from individuals once they no longer have legal capacity (the ability to understand and appreciate the consequences of his or her actions).

In such cases, persons with Alzheimer's disease and other dementias must rely on their surrogate decision-makers — usually a spouse, child, caregiver or other trusted individual — just as they eventually must do in all decisions of everyday life or medical care. Research study participation is not an exception to this necessary and beneficial dependency on caregivers.

Most discussions about protecting research participants address issues of risk. There is no single standard about what constitutes research that poses “minimal risk” versus “greater than minimal risk.” The Association believes that research considered “minimal risk” includes routine observations, data collection, epidemiological surveys, diagnostic interviews, blood draws and imaging scans.

By almost all standards, any study involving surgery is considered “greater than minimal risk” in the case of Alzheimer's disease and other dementias. However, the full spectrum of risk is more difficult to define. Federal agencies, such as the Food & Drug Administration (FDA), as well as the patient protection committees and internal review boards at research institutions, play an essential role in determining the risk of a particular study and exercise some control in educating participants and defining risks.

### ASSOCIATION POSITION

Written consent by the individual who is capable of making informed decisions should be the standard for participation in research. Informed consent may be provided through advance directives, which are legal documents allowing a person who still maintains legal capacity to document preferences related to future treatment and care. (Laws and processes related to advance directives may vary from state to state.) The Association affirms, however, that

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persons with designated disabilities who are no longer able to provide informed consent, and who did not in the past make clear their intention regarding research participation, should not be deprived of the potential benefits of promising research. Nor should they be denied the opportunity to make a contribution to science by participating in research that someday might help others. Surrogates should be able to make decisions regarding research participation without a formal legal device, as is the current standard of practice in dementia research programs.

The Association asserts the following three points regarding participation in research:

- For minimal-risk research, all individuals should be allowed to enroll and participate in research studies, even if there is no potential benefit to the individual. The consent of a surrogate decision-maker is acceptable even if the individual with Alzheimer's disease or another dementia did not address research participation in an advance directive.
- If the research presents greater than minimal risk and there is reasonable potential for benefit to the individual, the enrollment of all individuals with Alzheimer's disease or other dementias is allowable based upon consent of the surrogate decision-maker. The surrogate's consent can be based on either an advance directive about research participation or on the surrogate's judgment of the individual's best interests. The Association believes this second guideline will be wide in scope because most research into Alzheimer's disease and other dementias offers potential benefits to participants, thereby allowing for surrogate consent. This reliance on surrogate consent in all research of potential benefit to the subject is standard practice in dementia research programs worldwide.
- If the research involves greater than minimal risk and there is no reasonable potential benefit to the individual, only those individuals who (a) are capable of giving their own informed consent or (b) have executed an advance directive specifically addressing research are allowed to participate. In either case, a surrogate must be available to monitor the individual's involvement in the research.

Surrogates have a great responsibility overseeing the care of people with Alzheimer's disease and other dementias. When making decisions regarding participation in research, surrogates should consider the following principles.

- Surrogate consent should always be based on accurate facts about the risks and potential benefits of the clinical trial rather than on understatement of risks or burdens or exaggerated claims of benefit.
- Participants in all research should be protected from significant pain or discomfort. It is the responsibility of all researchers and surrogates to monitor a participant's well-being.
- Surrogates must not allow their hopes for effective therapies to overtake their critical assessment of the facts or diminish the significance of a participant's expression of dissent.

- A participant's dissent or other expressions of agitation should be respected, although a surrogate can attempt reasonable levels of persuasion. For example, a participant with dementia may initially refuse to have blood drawn or to take medication, but be willing to comply once a family member calmly explains the situation.
- Continued dissent by the participant requires withdrawal from the study, even when surrogates would prefer to see research continue.

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