Overview of the Topic

The determination whether research involves no more than minimal risk is a critical issue in IRB review. Minimal risk decisions are important for eligibility for exemptions or expedited review, waivers of consent or documentation of consent, research involving prisoners, and assessing risk in research involving children. Although not regulatory, minimal risk criteria are often used for assessing whether an amendment to research is minor. Despite its importance, the interpretation of the definition of and the determination of minimal risk is often controversial and variable.

The regulatory definition of minimal risk is: Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (45 CFR 46.102(i)). The definition is obviously open to broad, and legitimate, interpretation.

The first concept is the “Probability and magnitude of harm or discomfort.” Risks or harms may be physical (e.g. heart attack, toxic reaction), psychological (e.g. distress), social (e.g. reputation) or economic (e.g. employability, insurability). IRBs are usually very good at listing every possible risk, from low risks to high risks. But they must also consider the probability of a risk. For example, a risk may be very high (e.g. losing a job, death) but the probability of those risks in the context of the research may be extremely low and if low enough may still qualify as minimal risk. If the only risk is related to privacy and breach of confidentiality, the IRB may still consider it to be minimal risk if the researcher proposed reasonable and appropriate protections that the IRB feels would mitigate the risk.

The second concept is that these harms or discomforts are those which are “ordinarily encountered in daily life.” This could be risks related to such things as walking across the street, or riding in a car. Food tasting would usually fit into this category usually because eating is something people do every day. But as we all are aware, what is routine or ordinary is rapidly changing. Privacy and confidentiality in daily life is now subject to constant videotaping (estimates are that the average person is subject to video cameras 75-300 times per day), enormous data collection on everything we do on the internet, and the collection of phone records and text by organizations such as the National Security Agency – most of this uncontrolled, without our consent, and usually without our knowledge. IRBs must make their best decision on whether a risk is comparable to that ordinarily encountered in daily life.

The third concept is that harms or discomforts are compared to those “during the performance of routine physical or psychological examinations or tests.” Blood draws are usually considered in this category because they are done so routinely with few minor side effects. Again, this criterion is open to wide interpretation and the landscape of what is routine is changing. Procedures like lumbar puncture or biopsies are routinely done but are arguably not minimal risk. Approximately a million artificial joint replacements are done in the US each year which may meet the definition of routine but few would consider minimal risk. Again, the IRB must make its best decision on what is routine.

The bottom line is that the regulatory definition of minimal risk is imperfect and problematic. There is little doubt why there is so much variability in interpretations. Using the definition, IRBs need to develop their own working concept of minimal risk and make thoughtful, consistent decisions that they can be documented and defended. This is often accomplished by maintaining lists of research procedures determined to be minimal risk, and those deemed to be greater than minimal risk.

Subpart C sets a different definition and standard for minimal risk for prisoners: Minimal risk is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons (45 CFR 46.303(d)). This means that minimal risk for prisoners uses the comparison to healthy persons (non-incarcerated) not merely comparison to the health and risks of the prison population.

For research involving children Subpart D requires characterization of risk in several categories. The first category (46.404) is research not involving greater than minimal risk. The second (46.405) is for research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects. The third category (46.406) is for
research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield
generalizable knowledge. The 406 category is permissible if the risk represents a minor increase over minimal risk. You
can see that minimal risk decisions are very important in research involving children.

Physical risks, which often are present with biomedical research, are relatively easy to identify, quantity, and thus make
minimal risk determinations about. Social science research involves much different methodologies and much different
risks. For examples the risks related to anthropological research (e.g. group harms) or historical research (where the
information gathered is usually meant to be published with identification). IRB members reviewing these types of
social science research need to be knowledgeable in this area and understand the type and magnitude and probability
of risk in these areas. The vast majority of social science research is minimal risk and much is exempt. Of course, some
social science research does involve significant risks, such as studies involving domestic violence, criminal activities, or
socially stigmatizing information. The IRB needs to concentrate its attention and resources where the greater risks
occur. Overestimating risks is wasteful to IRBs, investigators and subjects. However, it is also important to remember
that even in research involving no greater than minimal risk, investigators and IRBs have an ethical obligation to treat
subject fairly and respect their rights (e.g. informed consent).

Questions for the IRB to Consider

When determining whether a research protocol is no greater than minimal risk, the IRB or reviewer should make the
following assessments:
1. Is the risk, harm or discomfort comparable to those ordinarily encountered in daily life or during the performance of
   routine physical or psychological examinations or tests?
2. What is the magnitude of the risk, harm or discomfort? In other words, how big do you think the risk is. You
   may want to routinely use a risk scale where 10 is the highest risk and 0-1 is the lowest.
3. What is the probability of the risk, harm or discomfort occurring in the research? In other words, how likely is it
   that the risk occurs, given the protections the researcher has proposed? Make this determination without regard
   to the magnitude of the risk. You may want to routinely use a risk scale where 10 is the highest probability and 0-1
   is the lowest probability?
4. IRB Decision: Consider your answers to the three questions above and make a determination of whether the
   research meets the criteria of “no greater than minimal risk.”
5. It is always a good idea to document how you made your determination.

Case Studies

Case 1. A protocol proposes to study alcohol and drug use in football and basketball athletes being recruited by
Division 1 schools. It involves a mail survey. While the athletes do not sign their name the surveys are coded and the
investigator keeps a secured master list to tract responses. Identifiers will be deleted once data collection is completed
in approximately 3 months. Paper surveys and electronic data are securely maintained. Is this study minimal risk?

Case 2. A protocol proposes to study the effectiveness of pet therapy in children (3-7) with developmental disabilities.
Children will play with dogs and cats for 30 minutes per day under researcher supervision. Paper surveys will be kept in
a locked file cabinet and data in password protected and encrypted computer files. Is this study minimal risk?

Prospective Thinking: Develop a risk scale like the one proposed
above and draw a plot like the one to the right.

- Discuss various examples of risks and try to plot each point.
- Discuss where you should draw the line for minimal risk.

Here are a few examples of research procedures to consider:
- Allergy skin testing in 11 year old children
- Confidential survey of sexual activity in college freshman
- Anonymous survey on soft drink preferences
- Survey of illicit drug use among company employees
- Deception study of color preferences of drug packaging

Note that this is merely a tool to help you think about minimal risk. Your best and final decision should always be made after
thoughtful contemplation considering all the facts.