What constitutes a component analysis? Give an example?

The IRB must determine there is proper justification of risks to subjects enrolled in clinical trials. Analyzing research risks for studies with multiple aspects is best accomplished by conducting a component analysis for each of the different components of the study versus the overall study risk.

In many clinical trials the different components include both therapeutic and nontherapeutic interventions. Both of these components should be evaluated independently and must pass each step to justify the potential risks. For example, a clinical trial with two arms in which all subjects receive optimized background therapy and are then randomized to either receive the investigational agent (therapeutic procedure) or placebo (nontherapeutic procedures) contains a mixture of components.
Therapeutic procedures offer the prospect of direct benefit to research participants, in addition to answering a research question(s). Clinical equipoise is satisfied if the IRB concludes that the evidence supporting the various therapeutic procedures is sufficient in that, expert clinicians would disagree as to the preferred treatment. The balance of risks and benefits for the therapeutic procedures should be equivalent to that associated with accepted practice. The IRB also considers if the benefit is applicable to all subjects exposed to the component.

Nontherapeutic procedures are designed solely to answer the research question(s). Are risks minimized by sound scientific design, i.e. avoidance of duplication of procedures already being performed for clinical purposes. Does the component contribute to answering the research question? Are the risks justified by the potential benefit associated with the knowledge to be gained? Judgment requires appraisal of social priorities and importance of the community member.

How to apply component analysis for studies involving children (21 CFR 50, Subpart D)

FDA recommends when applying Subpart D for child risk determinations for studies with placebo-controlled arms the component analysis of each arm is evaluated as opposed to a single evaluation of the possible benefits and risk for the entire study.

This may require two child risk determinations, one for treatment group and one for the placebo arm. For example, the treatment group could be greater than minimal risk but presenting the prospect of direct benefit to individual subjects (DHHS 46.405 / FDA 50.52). The placebo group in the same study would be greater than minimal risk, no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about subjects’ disorder or condition (DHHS 46.406 / FDA 50.53).

The signature line on the informed consent document should reflect the higher of the two risk categories (DHHS 408 / FDA 50.55). In the above example the consent of both parents would be required.