REPORT OF THE SCIENTIFIC/TECHNICAL ADVISORY COMMITTEE’S
CHILDREN’S RESEARCH WORKGROUP
MARCH 10, 2016

CHARGE:
What are the most important physical, psychological, and developmental
health outcomes to target and in which groups of children?

General perspectives:
The Children’s Research Workgroup believes that research to better understand the impact of
in-utero and childhood and adolescent exposure to 9/11 is of high priority in view of the
substantial and long-lasting mental and physical health effects that have been documented in
responders and survivors, and the results of studies among children with 9/11 exposures that
have been completed to date. Outcomes of interest include those already recognized as WTC-
related in adults, health effects that are currently emerging as potentially WTC-related in
studies of adults and children, and additional outcomes that may be unique to children and
adolescents. Although the spectrum of potential exposure to WTC dust is similar to that in
adults, especially for the children engulfed in the dust cloud, the majority of children exposed
in their homes, schools, and communities tended to have lower exposure levels than those of
worker populations employed at the WTC site, in whom the highest prevalence of WTC-related
conditions have been observed. However, as noted by Dr. Phillip Landrigan at the STAC
meeting on December 1, 2015:

“…..children have unique patterns of exposure that are very different from those of
adults. They breathe more air per pound of body weight per day, so anything
that’s in the air, children are going to be proportionally more heavily exposed.
Likewise, they drink more water and they eat more food. And then children engage
in behaviors that increase their exposures, like roll on the floor, and put their hands
in their mouths—and, all of those behaviors further increase children’s exposures.”

In addition to the risk factors for exposure noted by Dr. Landrigan, many children were
potentially exposed for longer periods of time than some workers at the site, especially those
children residing in homes with inadequate dust remediation and those living or attending
school in areas where demolition or removal generated re-suspended dust.

As further stated by Dr. Landrigan:
“…..children, in a sense, are at double jeopardy because they're not only more
heavily exposed pound for pound, they have greater sensitivity. One component of that sensitivity is that they’re not as able as adults are to break down and get rid of toxic chemicals. If an infant is exposed to an organophosphate pesticide, that chemical is going to remain in the infant’s bloodstream for 36 hours because the enzymes that we have have not yet developed in a newborn baby. Adults can break that chemical down in four hours. And if the chemical remains in the body for 36 hours, it has more time to exert toxic effects in the child’s body.

Especially in early development, during the nine months of pregnancy and in the first 12-24 months after delivery, there are periods of susceptibility, windows of sensitivity that have absolutely no counterpart in adult life. We first learned this the hard way sixty-some years ago in the thalidomide tragedy when women in Europe took the medication thalidomide, intended to suppress morning sickness during pregnancy, during the first trimester—which it actually did—but unfortunately, it was learned belatedly that thalidomide was a powerful teratogen. It hindered the development of limbs in the embryo and fetus and there was an epidemic of 8,000 or 10,000 babies born in Europe in the span of three or four years without arms, without legs because their moms had taken thalidomide during pregnancy, and the mothers were untouched. It was the first demonstration of the fact that, first of all, the toxic chemicals can get across the placental barrier from the mother to the baby and number two, that the fetus has unique vulnerabilities totally unlike the adult, and that experience has been repeated many times since then: diethylstilbestrol, ethyl alcohol, lead, mercury, pesticides, polybrominated diphenyls, brominated flame retardants.”

In addition to this exquisite vulnerability to developmental toxins prenatally and in the first few years of life, neurological, immune, and endocrine and other systems continue development throughout childhood and adolescence and may be uniquely vulnerable to adverse exogenous exposures. For example, women are uniquely vulnerable to developing breast cancer from ionizing radiation when they are exposed between puberty and first birth, a time when breast tissue has not undergone full differentiation. Prenatal, childhood, and adolescent exposure to low levels of endocrine-disrupting chemicals may also have greater and different health impacts than similar exposures in adults.

Dr. Landrigan continues:

“Finally, kids have a lot of future life, and we now understand that most chronic
diseases—whether it's cancer, heart disease, dementia—develop through multiple stages over long decades, and if somebody is exposed to a toxic chemical early in life, they have a lot more time to ultimately manifest the disease that is the consequence of that early exposure.”

With respect to trauma and other exposures that might have an impact on mental and emotional health, it is impossible to quantify the relative intensity for children versus adults because of their vastly different social and psychological constructs. As noted by Dr. Robert Brackbill at the Children’s Research Workgroup meeting on December 1, 2015:

“Children living or going to school near the WTC site may have witnessed the events at the time, the dust cloud, evacuation, panic, exiting the scene if they were in the vicinity. Children may have also experienced loss of a parent or other closely related person, evacuation from home and/or from school, changes in their social network and recurrent images from media coverage of the traumatic events.”

It is reasonable to think that children witnessing these events might be more vulnerable to psychological trauma than adults and have greater difficulty in regaining expectations of safety and stability in their daily lives. Because children’s mental and emotional lives are so intimately connected with the well-being of their parents, studies have demonstrated that children had increased risk of mental health symptoms if their parent was exposed to the WTC, even if the children themselves were not. Thus, children who were themselves affected by the disaster and had parents who were directly involved may be at higher risk of adverse mental health outcomes than those with only one or the other exposure.

One of the most salient features of WTC-related conditions is the high prevalence of co-morbidities, including both physical and mental health disorders. The etiology of these diseases is complex, and psychological and emotional distress can result in or exacerbate physical illness and vice versa. These complex inter-relationships that have been observed in many studies of WTC-exposed would likely also occur among children and adolescents. It will be important to study the impact of 9/11 on children and adolescents throughout their life course, and consider the potential influence of early life exposures on health outcomes that generally become evident later in life, including many chronic diseases. For example, the increased prevalence of cardiometabolic conditions in clinical studies of childhood survivors may presage increased risks for cardiovascular disease and diabetes in adulthood. It should also be recognized that many chronic diseases are related to behavioral risk factors such as tobacco
use, inactivity, and diet, and that behavioral risk modification and medical interventions may be effective in preventing or managing most chronic diseases. Therefore, if the WTC exposures are associated with increased risk of chronic diseases, there may be significant benefit to recognizing these associations and implementing interventions. Studies involving an in-depth physical health evaluation will be necessary to adequately assess such associations.

Although we make a strong case that potential health effects of WTC exposure in children and adolescents warrant additional study, it is important to note that we do not assume that substantial health effects will be found beyond those already documented. Although any studies in WTC-exposed children and adolescents are likely to have statistical power and other limitations that will make it difficult to interpret a negative result as completely reassuring, such studies may at least suggest an upper bound of risk for health effects examined. Such information will be important to the survivors or childhood and adolescent WTC-related exposures.

The Children’s Research Workgroup recognizes that the scope of research that may be possible in individuals who were exposed to the WTC as children and adolescents is constrained by a number of factors, including the time that has elapsed since the exposure and the availability of populations with well-characterized exposures for study. Because even the youngest children in 2001 are now 15 years old or older, it is probably not possible to do studies of short-term health effects or developmental or mental health outcomes in young children, most of which would require clinical examination, active observation, or measurement of the child. However, if a source of standardized records regarding educational testing, grades, absenteeism, behavioral problems, etc., were available for the relevant time period and could be linked with child’s residence and school attendance, it might be possible to do retrospective analyses comparing individual children before and after 9/11 or comparing populations of children by exposure status based on residence and schools attended. Such an approach would require identifying and obtaining access to a large system of school records with the relevant information.

Because it has been 15 years since WTC exposure, it will be difficult to conduct biological monitoring to reconstruct exposure, even if blood and urine samples could be collected now. This is particularly true for the majority of agents present at the WTC site and in the dust, which have relatively short half-lives in the body. If blood were to be obtained from a sample of individuals exposed to the WTC as children or adolescents, consideration could be given to
measurement of long-lived compounds, such as organochlorines, known to be present in dust samples, as well as biomarkers of persistent genotoxic or epigenetic changes. It would be important to collect, process, and store the blood in such a way to allow future testing as the state of the science advances. In addition, it is important to explore novel biomonitoring methods, such as analysis of metals and organic chemicals in deciduous and wisdom teeth, which may be useful for retrospective exposure assessment.

**Recommendations:**

**A. Importance of WTC Health Registry Population**

Children and adolescent survivors enrolled in the WTC Health Registry are an extremely important resource for understanding the health effects of WTC exposures. The registry used systematic sampling frames for identification of potential enrollees and did extensive outreach to recruit eligible populations. Because the recruitment and baseline questionnaire were completed relatively soon after 9/11, the information collected about exposures is likely to be more accurate than information that could be gathered now. The population of children and adolescents included in the Wave 1 survey represents no more than 10–20% of the target population and a wide range of exposure circumstances. Nonetheless, the population is limited in size (about 3,200 at baseline), and participation has declined in successive waves of surveys, resulting in concerns about statistical power and non-response bias. Because this cohort is such a valuable resource, it is important that every effort be made to sustain and renew participation in surveys and special studies.

As the importance of studying health effects in children and adolescents is recognized, additional special studies in the registry are likely to be proposed, raising the possibility that some registry enrollees will be contacted multiple times to participate in multiple studies, which could negatively impact participation. For this reason, and for the sake of efficiency and resources, it is appropriate to consider a more coordinated approach that could examine a broad range of mental and physical health outcomes in the Registry population. The appropriate framework might be a longitudinal study with periodic cross-sectional health assessments similar to examinations conducted by NHANES for the general population. The study could be undertaken as a collaborative effort between the Registry and a consortium of investigators with diverse expertise in the health outcomes to be examined. In addition to a core set of measures that would be collected in each round of testing, special studies could be proposed by investigators to detect more subtle, subclinical effects or follow-up on findings of
other studies. Such a prospective study, including clinical examinations and collection of blood
and urine samples, would likely provide the best opportunity to document the extent and
severity of long-term health effects in a cross-section of WTC-exposed children and
adolescents, and would also allow for the banking of biological samples for future testing as
more knowledge becomes available. Ideally, all registry enrollees who were children and
adolescents at the time of exposure would be invited to participate in order to maximize
statistical power and subgroup analysis. The Children’s Research Workgroup recognizes that
such a study would be resource-intensive and might require a different funding mechanism
than is used for individual grant proposals. We encourage NIOSH to conduct an analysis of the
feasibility and usefulness of such a study in the near future.

Recommendation #1

- Children and adolescent survivors enrolled in the WTC Health Registry are an extremely important resource for understanding the health effects of WTC exposures. Recommend that the WTCHP:
  - Make substantial efforts to sustain and renew participation in surveys and special studies.
  - Consider a coordinated approach that could examine a broad range of mental and physical health outcomes in the Registry population.
  - Develop a funding mechanism that would allow collaboration between the Registry and a consortium of investigators with diverse expertise.
  - Conduct an analysis of the feasibility and usefulness of a standardized health assessment approach, similar to NHANES, that could examine a broad range of mental and physical health outcomes in the Registry population prospectively.

B. Research Opportunities

The Children’s Research Workgroup believes that additional opportunities exist for research on
WTC-related health effects in exposed children and adolescents separate from the proposed
longitudinal clinical follow-up of the registry cohort. Such studies would most likely involve
relatively specific populations and specific outcomes. Examples of these were mentioned
during our meetings, and include additional studies on offspring of WTC-exposed women,
studies of mental and physical health effects in children of first responders affected by WTC-related conditions, studies of changes in school performance of individual children enrolled in area schools before and after 9/11 (if records can be made available), etc. Additional research studies should consider expanding exposure assessment to include ongoing air pollution from the recovery process and years rebuilding Lower Manhattan, e.g. up to 10,000 construction vehicles per month in 1.5 square miles and water tanks as a potential source of WTC contaminants after 9/11.

It is difficult for the Children’s Research Workgroup to offer guidance on the priorities for these studies. Likely the best way for NIOSH to identify such opportunities is to include the general area of childhood and adolescent health in their requests for proposals, and ensure that individuals with appropriate expertise are included in the review panels. Given all of the constraints noted for designing health effects studies 15 years after the event, the priority of any given study would depend on both the importance of the questions being addressed and the likelihood of the proposed study to answer them.

Recommendation #2
- Recommend that the WTCHP include the general area of childhood and adolescent health in their requests for proposals.
The Children’s Research Workgroup recommends that NIOSH create a distinct pediatric study section under the Zadroga research funding mantle so that pediatric proposals can be reviewed by experts with appropriate expertise in environmental health of children, and not compete in the review process, explicitly or implicitly, with responder proposals that have larger numbers of subjects, more exact exposure information, higher participation rates, and, in some cases, baseline data. The previously-described constraints on pediatric research opportunities prompt concern that proposed WTC studies of children may rank poorly when compared to responder studies, thereby diminishing their likelihood of being funded. We encourage NIOSH to consider a set-aside of funds during the next grant cycle that will specifically target meritorious pediatric research, especially since the window of opportunity to access these populations at younger ages is rapidly closing. We believe the WTC child and adolescent cohort provides a unique opportunity to understand the impact of environmental and social disasters on pediatric health, and addresses a national commitment to provide research and services to support the health of populations affected. In the event that a distinct pediatric study section is not created, at a minimum, we recommend that the primary and secondary reviewers in the NIOSH review process be pediatricians or other relevant health professionals with research emphasis in childhood environmental health. This will bring expertise and credibility to the review process.

Recommendation #3

- Recommend that the WTCHP create a distinct pediatric study section under the Zadroga research funding mantle so that pediatric proposals can be reviewed by experts with appropriate expertise in environmental health of children, and not compete in the review process, explicitly or implicitly, with responder proposals.

If a distinct pediatric study section is not created, at a minimum, we recommend that the primary and secondary reviewers in the NIOSH review process be pediatricians or other relevant health professionals with research emphasis in childhood environmental health.
D. Emphasize Physical Health Studies

Pediatric research of WTC exposures has emphasized consequences to mental health of children. It is essential that physical health effects of WTC exposures be examined as well, especially beyond the respiratory system. Pediatric research should emphasize multi-system impacts, examining a range of WTC physical health effects including respiratory illness, cardio-metabolic (including blood pressure), endocrine, neuro-development, autoimmune and cancer impacts. If feasible in retrospective studies, the developmental history, cognitive, and brain development of the affected children should also be examined. Clinical examinations may be required to assess an appropriate range of outcomes.

Recommendation #4

- Recommend that the WTCHP fund pediatric research that emphasizes multi-system impacts, examining a range of WTC physical health effects including respiratory illness, cardio-metabolic (including blood pressure), endocrine, neuro-development, autoimmune and cancer impacts.

E. Commit to Longitudinal studies

We encourage a commitment to longitudinal studies of physical and mental health. These types of studies have multiple advantages, including enhanced study validity, insights into the natural course of diseases and other outcomes, opportunities for intervention, and improved comprehension by the general public. They are especially important for understanding the effects of deleterious exposures in children, because children undergo relatively predictable development. Longitudinal studies are a sensitive way to assess departures from expected developmental paths. Particular attention should be paid to understanding critical windows of development, recognizing that these opportunities have diminished over time as the youngest child born after 9/11 approaches 15 years of age.

The current medical monitoring of WTC responders under the WTC Health Program represents in part a longitudinal research program to identify emerging WTC-related health conditions and to trace the evolution of recognized WTC-related diseases. The WTC Health Registry differs in methods, but represents the largest effort to perform longitudinal research on children affected by 9/11 exposures.

Support for longitudinal studies of children affected by 9/11 can have several target populations. As noted above, the WTC Health Registry is the best current basis for conducting a
longitudinal study, despite recognized limitations. Existing cross-sectional studies can be explored for conversion to cohort studies. Revival of old cohorts, such as the cohort of pregnant women at the time of 9/11 who were studied by Columbia and Mount Sinai investigators, is another possible option. Retrospective longitudinal studies of other child cohorts, reconstructed from other previous studies or from data sources extant on 9/11, should also be considered. These cohorts might include any births to from 9/11 responders up to 18 months after 9/11 (approx. 3/11/2003); the 18 months covers enough time to get through rescue and recovery time plus pregnancy and delivery. This description would cover both women who worked on or near the WTC site (direct exposure) and female partners of first responder women who had exposure through clothing, gear, etc. (secondary exposure).

**Recommendation #5**
- Recommend that the WTCHP commit, to the extent possible, to longitudinal studies of physical and mental health

**F. Formation of Study Consortium**

Given the severe shrinkage in the number of children currently or “recently” involved in studies (<1,000 in the WTC Registry; <700 in the Hoven WTC Registry-based study; and about 200 in the Trasande survivor clinic study), it appears that the optimal way to study multiple outcomes is through a coordinated research consortium that focuses on a single cohort.

**Recommendation #6**
- Recommend that the WTCHP fund a coordinated research consortium that focuses on a single cohort.

**G. Enhance the Range and Participation in WTC Pediatric studies**

Cohort Reconstruction Feasibility studies: A number of child cohorts or potential cohorts have been cited or published, but appear to be inactive or to never have been studied. These include 1) high school students in WTC zone; 2) elementary school students in the WTC zone; 3) children born to women who were pregnant on 9/11; 4) children of WTC workers; 5) child WTC Registry participants who have dropped out; and 6) others. Limited short-term grants to attempt cohort identification, location, and willingness to participate in studies will answer outstanding questions about whether unexamined opportunities to learn more about
childhood effects of 9/11 can be addressed 15 years after the event. If found to be feasible, new studies of health effects among these cohorts could be initiated.

The Children’s Research Workgroup additionally believes that NIOSH should consider use of appropriate incentives to the WTC children cohort to enhance their ongoing participation.

**Recommendation #7**

- Recommend that the WTCHP fund limited short-term grants to attempt cohort identification, location, and willingness to participate in studies to answer outstanding questions about whether unexamined opportunities to learn more about childhood effects of 9/11 can be addressed 15 years after the event.

**Recommendation #8**

- Recommend that the WTCHP consider use of appropriate incentives to the WTC children cohort to enhance their ongoing participation.

**H. Blood-banking and biomarkers**

State-of-the-art methods for blood banking and preservation of cells from WTC-exposed children should be supported so that DNA, RNA, proteins, and long-lasting toxins can be studied in the future. This should be completed for the Registry cohort and other WTC child and adolescent survivors.

**Recommendation #9**

- Recommend that the WTCHP support blood banking and preservation of cells from WTC-exposed children using state-of-the-art methods so that DNA, RNA, proteins, and long-lasting toxins can be studied in the future.
I. Understanding Research Results

In responding to its charge, the Children’s Research Workgroup found it challenging to
understand the full body of child-related WTC research, and how the completed and ongoing
studies overlapped in cohorts, outcomes, and methods. This was in part due to the lack of a
dedicated and integrated review of the topic, which is not designed as part of the STAC
advisory process. NIOSH is doing an outstanding job of communicating its research program
within the WTC research community and also to the larger public health community, especially
through an excellent website (http://www.cdc.gov/wtc/wtcresearch.html). It would be
additionally helpful, especially as WTC-related research has grown with hundreds of
publications at present, to assist researchers, practitioners, and the general public alike, if
NIOSH could develop various means to communicate how the various cohorts, study methods,
and outcomes inter-relate, and what the accumulated findings are to date. Funding systematic
reviews on a periodic basis would contribute to the desired clarity and could be part of the
extramural research funded by NIOSH under its WTC research program.

There is also the need for communication to the health care community of up-to-date WTC
research findings and their implications for practice. This could take the form of updated WTC
pediatric care and treatment guidelines.

Recommendation #10
• Recommend that the WTCHP develop various means to communicate how
  the various cohorts, study methods, and outcomes inter-relate, and what
  the accumulated findings are to date.

Recommendation #11
• Recommend that the WTCHP communication to the health care
  community up-to-date WTC research findings and their implications for
  practice, such as through updated WTC pediatric care and treatment
  guidelines.

J. Research Design for Study of Disaster Health Effects among Children

The Children’s Research Workgroup takes note of the limitations in the past and current ability
to study disaster-related effects among the children involved with the 9/11 event and its
aftermath. We recommend conducting a formal study of missed opportunities for childhood
study from 9/11. This would include a roadmap for the post-disaster setting about how to
Recommendation #12

- Recommend that the WTCHP conduct a formal study of missed opportunities for childhood study from 9/11, including a roadmap for the post-disaster setting about how to identify and enlist exposed childhood subsets; how to approach exposure measurement; and the nature, range, and tools to use to study health effects.