BOSC REVIEW OF CHILDREN'S HEALTH ROADMAP ANNUAL REPORT

List of Acronyms

AAP	American Academy of Pediatrics
ACE	Air, Climate, and Energy
BOSC	Board of Scientific Counselors
CDC	Centers for Disease Control and Prevention
CEH	Children's Environmental Health
CSS	Chemical Safety and Sustainability
EJ	Environmental Justice
EPA	U.S. Environmental Protection Agency
ES	Executive Summary
FY	Fiscal Year
HHRA	Human Health Risk Assessment
HS	Homeland Security
IWG	Implementation Working Group
MCH	Maternal and Child Health Bureau
NIH	National Institutes of Health
NRC	National Research Council
ORD	Office of Research and Development
PEHSUs	Pediatric Environmental Health Specialty Units
PIPs	Pathfinder Innovation Projects
SAP	Scientific Advisory Panel
SHC	Sustainable and Healthy Communities
SmARTI	Smart Acceleration of Research Through Investment Awards
SSWR	Safe and Sustainable Water Resources
STAR	Science to Achieve Results
StRAP	Strategic Research Action Plan

Background

The October 12, 2016 Draft Children's Health Roadmap Annual Report (draft Annual Report) provides a comprehensive summary of the progress made during FYI 2016. There has been excellent progress towards successful integration and implementation as articulated in the Report. The Board of Scientific Counselors (BOSC) also notes evidence of excellent coordination across the Office of Research and Development (ORD) research programs on this issue, and strong evidence of outreach to partners and stakeholders. The excellent work of ORD is, however, seen by a relatively small group of people when it has relevance and power to affect so many more and, in turn, be guided by, and benefit from dissemination to a broader audience. It is, therefore, important to ensure that the Annual Reports and the research they represent are accessible to a range of target audiences, including the public. The BOSC suggests some opportunities for clarification and consistency of reporting. In future Annual Reports it would also be helpful to include sections on the progress toward incorporation of social science into the research area, the strategy used to identify emerging issues, and a more explicit discussion of planned next steps for the research.

This report was drafted by the following members of the BOSC Executive Committee:

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Within the past year, the U.S. Environmental Protection Agency's (EPA's) ORD released its cross cutting Research Roadmaps (https://www.epa.gov/research/research-roadmaps) to describe current and facilitate future integrated ORD research across four prominent cross-cutting areas: Nitrogen and Co-Pollutants, Children's Environmental Health (CEH), Environmental Justice (EJ), and Climate Change. The cross-cutting Research Roadmaps are not stand-alone research programs; rather, they integrate research in these priority areas across ORD's six Strategic Research Action Plans (StRAPs) (https://www.epa.gov/research/strategic-research-action-plans-2016-2019) developed by the six ORD National Research Programs: Air, Climate, and Energy (ACE); Chemical Safety for Sustainability (CSS); Human Health Risk Assessment (HHRA); Safe and Sustainable Water Resources (SSWR); Sustainable and Healthy Communities (SHC), and Homeland Security (HS). This integrative vision focuses ORD's investment on areas where EPA can play a significant leadership role and ensures that cross-cutting research is the foundation of sustainable decisions and actions in these four priority areas.

This first issue of the Annual Reports for each of the Research Roadmaps captures progress on research goals and activities during Fiscal Year (FY) 2016 (FY16; October 1, 2015 to September 30, 2016). The Annual Reports highlight successes and challenges of implementing an integrative approach to ORD's cross-cutting research. The Annual Reports also provide a preview of research activities in the upcoming fiscal year.

Process

The CEH Roadmap was completed about 18 months ago. Progress made in FY 2016 was excellent and included: (1) more than 290 abstracts, book chapters, peer-reviewed publications, posters and presentations; (2) direct relevance to Agency decisions related to pesticides, endocrine disruptors, and other environmental issues relevant to children's health; (3) research that supported important children's health issues related to lead in drinking water, indoor air quality, and Zika virus; (4) establishment of five new Children's Health Research centers studying asthma, autism, leukemia, the microbiome, and nonchemical stressors; (5) outreach to the US National Academies of Science, Engineering and Medicine for scientific advice on low dose effects and microbiomes; (6) links to program and regional partners through the CEH Implementation Working Group; and (7) innovative strategies to stimulate and encourage researchers far afield to become engaged in relevant children's environmental health research, this is a good investment in the future.

Charge Questions and Context

Charge Question 1. Comment on areas of successful integration and implementation as articulated in the related Roadmap. This may include, but is not limited to, the following:

- Levels of commitment to Roadmap recommendations as incorporated into the ORD StRAPs;

- Coordination across ORD's six National Research Programs;
- Communication and outreach to partners and stakeholders; and
- Areas of innovation

Charge Question 2. Provide suggestions for improving implementation of the roadmaps and research integration across the National Research Programs.

- Are there additional opportunities for implementation or integration not highlighted in the annual report?
- Does "The Year Ahead section" adequately describe the next steps and short-term research areas and commitment?

General Comments on Structure and Readability

The BOSC found that the draft Annual Report provides substantial evidence of impressive, impactful research relating to CEH. It is not clear, however, who the intended audience is for this report. It is written at a level that would make it very difficult for even a sophisticated member of the public to understand. If the public or policymakers are an intended audience, and to make the report clearer and more compelling for any reader outside of EPA, certain changes should be made. For example, the Executive Summary (ES) contains the terms "vasculogenesis", "in silico", and "systematic scoping review", all of which would be challenging to many readers. In addition, the ES on p. vii includes the phrases: "computational models of estrogen receptor activity" and "in silico models of reproductive development", raising the question of how "computational models" differ from "in silico models"? In the body of the report, it is important to be sure to spell out terms and acronyms when they first appear, including the names of the other National Research Programs (p. 6). Similarly, in some places in the Executive Summary numerous references are inserted in parentheses in the middle of sentences, making the text difficult to read; this is particularly true in the last full paragraph on p. vii. Minimizing the use of references in the ES is preferable for readability. The BOSC notes that the "Research Highlight" text boxes in the Annual Report are an excellent feature. It would be appropriate to include more of these. However, the same concerns about technical level and readability apply to the highlights as to the text of the report.

In general, the section on Accomplishments should follow a consistent format. Each subsection should begin with 1-2 sentences summarizing why the issue is important, since some people will not find that immediately obvious. For example, on p. 2-3, "Certification of Pesticide Applicators", "Endocrine Disruptor Screening Program" or "Perchlorate Dose-Response Modeling" don't necessarily convey immediately why these are important issues for the average person, so the first sentence or two of each should concisely convey the relevance of the item. The subsection on "Microcephaly and Zika Virus" is an excellent example of providing appropriate introductory context, as is the subsection on tire crumb. Next, the ORD contribution should be described, preferably in a series of bullets. At the end of each subsection, there should be a sentence stating the current status of the issue and next steps (where relevant). A consistent format and some attention to making each subsection clear and readable will improve the quality of the Report considerably.

The subsection on certification of pesticide applicators blurs directly into the Scientific Advisory Panel (SAP) review of chlorpyrifos, which is a separate issue discussed in the following subsection. The relevant sentence on p. 2 should be moved to the correct sub-header. In the subsection on chlorpyrifos, the title refers to organophosphates generally, which isn't accurate, and highlights "Retention of Safety Factor" in the header, which will be meaningless to most people who aren't familiar with the intricacies of the Food Quality Protection Act. Instead, this subsection should be written so that it the header is clear and

accurate, and the paragraph (or bullets) clearly describe the relevance of this important issue and the ORD contribution.

It might also be helpful to get a writer to create a lay summary of the Annual Report. Such a summary would contribute to environmental health literacy among the general public and among pediatricians, teachers and parents. This relates directly to the statement in the roadmap which says: *EPA conducts and supports children's environmental health (CEH) research to inform regulatory decisions and to support community decision-making that promotes sustainable, healthy environments for children.* This may also benefit and enable students to become more aware of the environmental health issues of our day and incorporate that knowledge into their academic pursuits, become engaged with one of the ORD Innovative programs and become the researchers and leaders of the future.

Levels of Commitment

The annual report demonstrates excellent commitment to the children's health StRAP, as well as to other StRAPs that are relevant to children's health from other program areas and cross-cutting areas. Specific examples of how the Annual Report demonstrates a commitment to the various StRAPs include:

- In the development of indicators for and spatial visualization of community resilience and vulnerability to climate change;
- In public health impacts of air pollutants to susceptible populations, especially asthmatics, and development and application of air quality modeling tools; and
- In examining exposure and early-life vulnerability to chemicals, and cumulative risk assessment.

Coordination across National Research Programs

The CEH Implementation Working Group (IWG) provides a good focal point for coordination across the six research programs, as well as with EPA program and regional offices. The IWG also provides an avenue for regular, on-going communication with, and outreach to, partners and stakeholders within the Agency. IWG members include 16 representatives from ORD, but it's not clear if each of the six research programs is represented. It would be helpful to identify the affiliations of each of the IWG members in the document. Active membership by representatives from most, if not all, of the six research programs in the IWG would help continue and support the integration across programs. It is also important to evaluate and make explicit links to the other cross-cutting roadmaps, particularly including those on Climate Change and Environmental Justice, both of which are issues with significant children's environmental health components; these links could also be through the IWG, but they are not evident from reading the Annual Report or scanning the list of IWG members.

Communication and Outreach

The BOSC noted with approval that the ORD efforts on children's environmental health in FY 2016 have involved numerous and significant scientific communications at meetings and conferences, targeted meetings for ORD partners, and numerous peer-reviewed publications. Of particular importance are the groundbreaking and highly relevant research efforts on prenatal exposures, developmental neurotoxicity, nonchemical stressors and epigenetic modification that are particularly important as an academic and practical approach to children's health, growth and development. Even more creative and more comprehensive is the consideration of a "holistic understanding of the relationship between early-life environmental exposures and well-being across the lifespan". Continuing the efforts to disseminate this

work in the scientific community will be important going forward, and this will require staff to travel and to allocate effort toward publications and presentations.

In addition to scientific presentations, it would be beneficial to communicate more about ORD's children's health research activities to a general audience, including through presentations to general audiences and publications targeted to the lay reader. To this end, the ORD portfolio could include a translational or communication component that focuses on how to take this exciting and clinically relevant information into the broader field of children's health and development and translate and transform it into intelligible information for professionals as well as parents and the lay public.

The Pediatric Environmental Health Specialty Units (PEHSUs) have the role of conducting children's health outreach and communication and supporting translation from research to practice. This network of 10 centers is also a unique resource for gathering information and concerns from the public and professionals about children's environmental health. The PEHSU network can serve to help in the identification of emerging issues and research needs that ORD can then consider acting on, and can also help ORD to communicate its research findings to a broader audience. Perhaps participation in the PEHSU network annual meeting or finding a way to combine meetings such as is done with the PEHSUs and NIEHS on a regular basis, could help achieve the goal of bidirectional communication. It would be valuable to show clear communication between the PEHSUs in each region and ORD to inform innovative research efforts and ensure relevance. It should also be noted that the PEHSU's are linked with the American Academy of Pediatrics (AAP) and as such have a direct link with its publications and information dissemination operation that reaches 64,000 practicing pediatricians across the country. Of interest is that the AAP has a focus on early brain development (see ORD research in the prenatal and neurotoxicity areas) and poverty (ORD interest into nonchemical stressors) in its 2016-2017 national strategic plan – see https://www.aap.org/en-us/about-the-aap/aap-facts/Pages/AAP-Facts.aspx.

The issues of Climate Change and Environmental Justice are of major national and international importance to our global society. It would, therefore, be a good idea with these and other environmental issues of global significance, to reach out beyond the EPA universe and partner with other federal agencies like the Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH) or even the Maternal and Child Health Bureau (MCH) in reference to children, much as efforts to address Zika have crossed Agencies as stated in the ES. The Zika response could be an example for other crosscutting issues, like children's health, EJ and climate change.

Areas of Innovation

The Pathfinder Innovation Projects (PIPs) program, Smart Acceleration of Research Through Investment Awards (SmARTI) awards program, and Science to Achieve Results (STAR) Grants are critically important for encouraging innovation and driving cutting edge research. Furthermore, these areas of innovation are particularly exciting because they stimulate and encourage young researchers to explore new and creative ideas – this is the best way to not only develop new information but to cultivate future leaders – this should be strongly supported and encouraged. In addition, the Children's Environmental Health and Disease Prevention Research Centers represent another rich potential for new ideas, new research and new findings as well as cultivating future leaders on a meaningful scale.

Areas of particular relevance to advancing the knowledge and practice in children's environmental health are the projects looking at evaluating and understanding the potential effects of chemicals during pregnancy on fetal growth and development in the *Virtual Tissues Modeling Research Project – Integrating EPA's Intramural and Extramural Research* – this is an area with great promise and potential. The prenatal

period is a critical time of vulnerability in child development, and multiple projects in the CSS program area are focused on evaluating child-relevant exposures and hazards, with a focus on the prenatal period. For example, the virtual tissues modeling includes work focused on early-life neurodevelopment.

Two areas highlighted in the report include innovative reports from the National Academies, including, *Unraveling Low Dose: Case Studies of Systematic Review of Evidence,* which demonstrates a collaboration under the auspices of the National Research Council (NRC) in developing a strategy for evaluating evidence of low-dose adverse human effects that act through an endocrine-mediated pathway.

Also important are the two projects focusing on the microbiome with the National Academies of Sciences, Engineering, and Medicine, on the *Microbiome of Built Environments,* and with the NRC on *Advancing Understanding of the Implications of Environmental-Chemical Interactions with Human Microbiomes.* These examples of partnerships in critical areas of research represent areas of innovation with strategies and approaches that should continue and grow at ORD.

Highlighting indoor air and health as an emerging area of innovation and integration across ORD's National Research Programs (including indoor air and climate [ACE], healthy schools and science to support healthy Tribal environments [SHC], indoor exposures to consumer products [CSS], and the microbiome of built environments [across ORD and with EPA's Office of Radiation and Indoor Air]) is laudable. However, page 6 of the draft Annual Report should be edited because this area of indoor air research is not "An emerging area of research interest" (suggested edit: "An emerging area of research integration"). Indoor air quality is not an emerging issue as stated on page vii "emerging issues of concern, such as indoor air quality." Indoor air quality has been an issue of concern for decades, so it is important not to portray it as a new issue.

Indoor air quality is important, and this is a critical research area related to children's environmental health. In this context, Table 4 presents STAR grants addressing CEH research, including seven projects focused on indoor air quality in schools. Although the focus of each of these projects likely differs, and they are being conducted in a range of geographic areas and populations, a casual reader might see these studies as redundant. It would be helpful to include some additional explanation in the paragraph describing Table 4 to highlight the reasons why it is important to have seven separate STAR-funded projects focused on indoor air quality in schools. It also would be helpful to understand how the seven school projects provide opportunities for research integration. It is important to highlight the fact that children spend a great deal of time in school: on average 5 hours during the day for 5 days a week and on average 40 weeks a year – that is about 1,000 hours a year for 12 years – so the indoor air quality and other environmental aspects of school buildings are highly relevant to children's environmental health. In 2014, the National Center for Education Statistics found that more than half of U.S. public schools reported needing to spend money on their school buildings to bring them up to good condition. There is a clear relationship between the condition of school facilities and factors critical for student academic performance. See http://centerforgreenschools.org/state-our-schools. Furthermore, this issue is relevant to the Environmental Justice Roadmap, as there is a disparity in the quality of school buildings in poor vs more affluent neighborhoods which again brings into focus the impact of poverty, nonchemical stressors, cumulative environmental burdens, environmental heath disparities and EJ issues.

Opportunities for Implementation and Integration

Incorporation of social science into CEH programs is not highlighted in this report, although some examples are discussed (particularly in the discussion of lead research). Given the current emphasis on incorporation of social sciences, perhaps additional discussion and examples can be presented in the FY

2017 annual report. This will be particularly important in providing a perspective on children's health and well-being in the context of the family, the community and the built environment – in reality taking on an ecological context. This more integrated view of children's health could benefit from a social science perspective.

The Executive Summary states that the report identifies emerging issues or data needs that could inform future research efforts (p. vi). The BOSC sees some examples of emerging issues in the report, but failed to find a specific section that discusses how ORD identified and evaluated emerging issues in CEH in FY 2016. Is this done through the IWG? A brief discussion of the process for identifying emerging issues would add to the narrative on ongoing implementation of the roadmap.

There is very impressive evidence in the annual report of research that is increasing knowledge in exposure, toxicology, and epidemiology. What about in the areas of: (1) Root causes or conditions leading to exposure? (2) Understanding the magnitude and extent of emerging problems? (3) Identifying and evaluating solutions or approaches to prevent/reduce exposures? The discussion of lead research provides some good examples of this type of research. In other words, it would be important to develop an integrative approach to the relationship between environmental factors and the impact on health, such as considering an ecological framework for the environmental factors and individual and community well-being for the health impacts. The next annual report might provide more examples of this type of systems approach (root causes—magnitude of problem—understanding of effects—exposure prevention/minimization—treatments or other resolutions) in other areas of research.

One particular area of research integration that the BOSC finds especially important centers on the evaluation of the impacts of poverty and non-chemical stressors that predispose, complicate and confound the exploration of children's health - this issue is at the nexus of the Children's Health and the Environmental Justice Roadmaps and would be a critically important area for more research integration. In fact, ORD should be commended on its recognition of, and research in, this critical emerging area of focus. We encourage further and deeper research into these areas as they represent a previously-neglected area. There is a great need to address this major source of environmental health disparities and thereby promote environmental health equity. The impact of combined and cumulative adverse social and chemical stressors on children's health is great and the research challenges are monumental, making this an area where ORD could have major impact.

The *Challenges and Opportunities* section does provide promise of new approaches and new technologies that will address important issues related to children's environmental health. These include:

- Protection of potentially exposed or susceptible subpopulations: this is the most important element that relates to children among other vulnerable and relevant populations, including pregnant women and families living in circumstances of social and economic disadvantage.
- Focus on exposure characterization, predictive capacity and the interactive *Chemistry Dashboard* with information for over 700,000 chemicals and the potential to examine and characterize their potential toxicity.

Next Steps and Short Term Research Areas and Commitment

In general, the sections on "Progress and Emerging Opportunities" in the ES and the section on "The Year Ahead" in the body of the report are rather scanty and vague, describing near-term research efforts in general terms and merely listing the ongoing research and proposed meetings without conveying a sense of energy and excitement focused on developing new partnerships and promoting children's

environmental health in new and exciting ways. It would be preferable to provide more specifics, if possible, on ongoing and planned research activities for the coming year. If possible, a table or listing of specific activities and projects would be helpful to convey a more complete and compelling picture. It might be appropriate to add a focus in this section on identifying additional opportunities to integrate with the other cross-ORD Research Roadmaps on Climate Change, and Environmental Justice and also add more focus on children in the context of families and communities.

Recommendations

1. **Recommendation 1:** Explore greater integration and focused research evaluation on cumulative environmental insults, both chemical and non-chemical. This research should include the impacts of poverty and non-chemical stressors, in combination with chemical and environmental stressors on children's health. The approach to children's environmental health should include a perspective on the family and the community – this context is critical to determining the impact of environmental factors on child health and well-being.
2. **Recommendation 2:** Continue to consult with the National Academies of Sciences, Engineering, and Medicine, and strengthen collaborative relationships with other agencies (such as CDC, NIH, and Education), and with the PEHSUs to explore cross cutting issues that relate to children's environmental health and improve communication with the public.
3. **Recommendation 3:** Develop publications and presentations on ORD's Children's Health research activities for lay audiences. ORD could benefit from more staff with expertise in communication with the lay public and research translation. Alternatively, ORD can work with other agencies and organizations to accomplish this goal, e.g., with the PEHSU network or with the AAP.
4. **Recommendation 4:** In the 2017 FY Annual Report, provide a summary of how the social sciences are being incorporated across CEH and provide a few examples. The inclusion of social sciences into the range of activities of ORD will go a long way to translate the basic science that is the staple of ORD into the practical realm of the psychological, social and sociological relevance of the environment for the child, the family and the community.