# Draft Translational Research Framework for Environmental Health Sciences

**Proposed by: Division of Extramural Research and Training (DERT), National Institute of Environmental Health Sciences (NIEHS)**

The Division of Extramural Research and Training at the National Institute of Environmental Health Sciences (DERT/NIEHS) recognizes the need for a translational research framework that 1) captures all the nuances of environmental health research, with additional details added at the more "basic" end of the research spectrum; 2) represents the full spectrum of the research our grantees conduct; and 3) provides a common language for describing translational research in the environmental health sciences.

This document describes a draft translational research framework for the environmental health sciences. Recent efforts to evaluate translational research at NIEHS have identified challenges with existing frameworks. This document is an effort to build and expand on existing translational research frameworks so they are more applicable for translational research trajectories in environmental health science.

## Emergence of "Translational Research" at NIH

NIEHS supports translational research in many high-profile extramural research programs (see box). These diverse programs support research at all biological levels, from sub-cellular through cell systems, organs, whole body, community and population levels. A range of settings (*in vitro, in vivo, in situ*) and model organisms are also represented. Environmental health science research often focuses on minimizing or preventing exposure to environmental contaminants, or interventions to address the human health outcomes associated with environmental exposures.

The term "translational research" was introduced nearly 2 decades ago and has been used in a variety of settings across many NIH Institutes, Centers and Offices. Frameworks that describe the translational research concept have evolved from a simple translation from "basic" to "applied" research (e.g., Sung et al. 2003), to more complex models involving translation into clinical practice and public health impact (Khoury et al. 2007). Trochim et al. (2011) provide a succinct overview of the evolution of the concept (Figure 1),

The Trochim et al. (2011) schematic (Figure 1) identifies up to four translational layers, abbreviated T1 through T4. Earlier translational research frameworks have less nuance (T1-T2) compared to later models (T1-T3 or T4). None of the models presented by Trochim et al. include "research translation" to communities or lay audiences. Each of the frameworks presented expands on the nuances of the approaches and research that are included and potentially "counted" as translational research.

**Examples of NIEHS Extramural Research Programs with Translational Research Components**

Breast Cancer and the Environment

Children's Environmental Health Centers

Environmental Health Science Core Centers Program

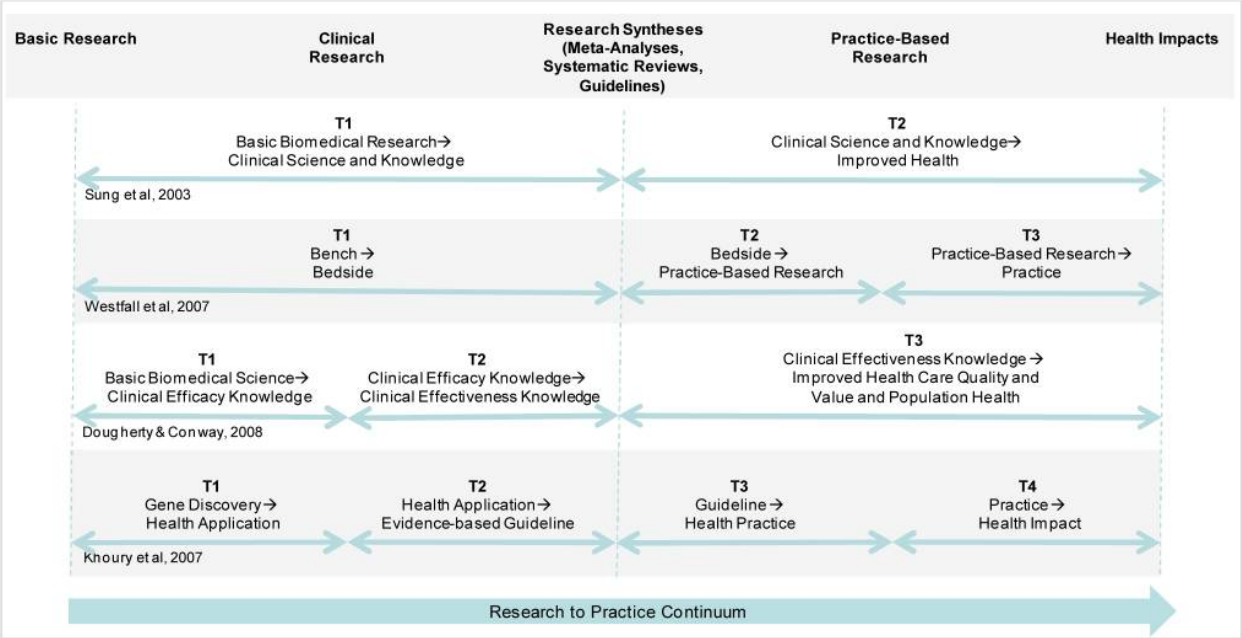
Superfund Research Program

Outstanding New Environmental Scientist (ONES)

Partnerships for Environmental Public Health

Virtual Consortium for Translational/Transdisciplinary Environmental Research (ViCTER)

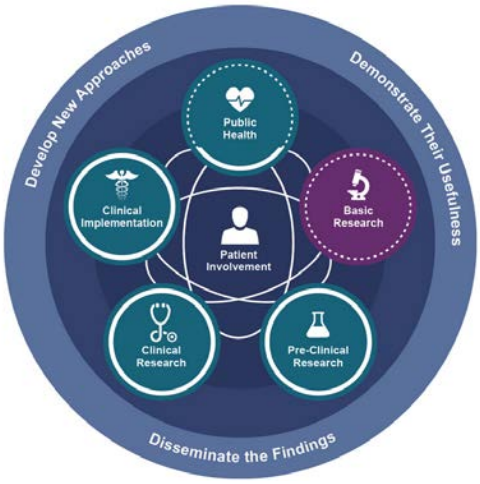
**Figure 1. Comparison of Four Major Translational Research Frameworks** (Trochim et al. 2011, used with authors permission) (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3125608/figure/F5/)




The NIH-supported Clinical and Translational Science Awards (CTSA) have taken these concepts a bit further to identify five different research areas, or "landmarks," that represent the scientific process and defined translational research as research that **bridges or connects two or more of these areas or landmarks** (Figure 2) (Drolet and Lorenzi 2011):

T1 – basic biomedical science or discovery – cellular, animal, human, proof of concept
T2 – human application – prevention research and treatment identification and development
T3 – clinical treatment, patients – practice implications, individual treatment of individuals
T4 – practice – clinical guidelines, public health interventions, community (policy, laws, regulations, etc.)
T5 – local and global communities – public health impact, population level

**Figure 2: Translational Science Spectrum as defined by the National Cancer for Advancing Translational Sciences** (http://www.ncats.nih.gov/translation/spectrum)



It is also important to note that translational research is different from research translation, which generally refers to the communication of scientific information to non-scientific audiences – especially in a way that is tailored for those audiences. NIEHS has long championed the need for translating research broadly and going further to involve communities of all types (local, regional, national, global, virtual) in research.

## Translational Research at NIEHS

NIEHS has a rich history of supporting translational research through many different extramural research programs (see box on page 1), within our intramural research programs, and through the work of the National Toxicology Program. Each of these programs has its own concept of translational research, but they all follow the basic concept of ensuring that the research we fund ultimately informs advances in human health.

These diverse research programs support research at all biological levels, from sub-cellular through cell systems, organs, whole body, community and population levels. A range of settings (*in vitro, in vivo, in situ, in silica*, etc.) and model organisms are also represented. Environmental health science research often focuses on minimizing or preventing exposure to environmental contaminants, or interventions to address the human health outcomes associated with environmental exposures.

Recently, the extramural program evaluated the translational research components of the Environmental Health Science Core Centers program (Core Centers). This program provides environmental health science infrastructure to researchers across the US. Since the October 2005 Core Centers funding opportunity announcement (http://grants.nih.gov/grants/guide/rfa-files/RFA-ES-05-008.html) the centers have been required to support an Integrated Health Sciences Facility Core to advance translational research. In the 2006 funding opportunity announcement, NIEHS began to define translational research as "as efforts along the spectrum of steps that transform scientific discoveries arising from laboratory, clinical, or population studies into clinical or population-based applications to reduce disease incidence, morbidity, and mortality" (http://grants.nih.gov/grants/guide/rfa-files/RFA-ES-06-010.html). In 2015 we completed an evaluation of the Core Centers program, in which we assessed 1) the types of translational research the Centers support, 2) the strategies they use to support translational research, and 3) the impacts of the translational research they support.

In defining the concept of translational research for the evaluation, we drew on the definitions from the funding opportunity announcements. We also incorporated the idea of bridging from one research area to another that was noted in a 2008 article from NIEHS staff, who noted that, *"translating research and patient data should be viewed as an interconnecting and multidirectional network, with information that flows back and forth among basic research scientists, clinicians, epidemiologists, engineers, and policy makers. Key to this process is the transfer of knowledge (information) among these different groups…"* (Denholm and Martin, 2008, p2).

Our evaluation was also informed by the National Center for Advancing Translational Sciences (NCATS) translational research framework (Figure 2) and a checklist created by the Clinical & Translational Science Institute of Southeast Wisconsin (2013) to help us operationalize a definition of translational research. The evaluation team, comprised of several external advisors, identified several challenges with the NCATS model. One key concern was that many activities presented as "basic" or "T1-T2" projects because there was not enough nuance in the checklist to capture what we inherently felt should be counted as translational research. Another challenge was the primarily clinical and patient focused perspective that is less applicable to much of NIEHS-funded research. In addition to challenges with the model itself, the evaluation team struggled with how grantees report their translational research. Reporting mechanisms, such as annual progress reports or publications, don't encourage grantees to describe the longitudinal nature of translational research, or the dynamic interactions and processes that are inherent in translational research. The evaluation team

identified many exemplary stories of translational research as part of the Core Centers evaluation, and also recommended that NIEHS adapt the existing translational research models to tailor them to the environmental health science context.

Since the completion of the Core Centers evaluation in the fall of 2015, extramural research staff at NIEHS has been working on adapting the existing translational research framework. Our approach was to compile and analyze a diverse set of examples that exemplify translational research for environmental health sciences. We focused on key translational landmarks and the bridges that connect them. Particular attention was given to research activities that are typically categorized as 'basic' or 'T1' using a traditional framework.

Our conversations led to the model that is proposed in subsequent sections of this document. The framework is intended to provide environmental health researchers with some common "sign posts" with which to tell their translational research story. Not every story will include all the sign posts, but ideally the landscape we propose is both broad and flexible enough for all kinds of research to fit. We have developed several detailed examples that illustrate how the framework can be used to describe translational research for environmental health science. One example is included in this document, and others are available at (http://partners.niehs.nih.gov/trf).

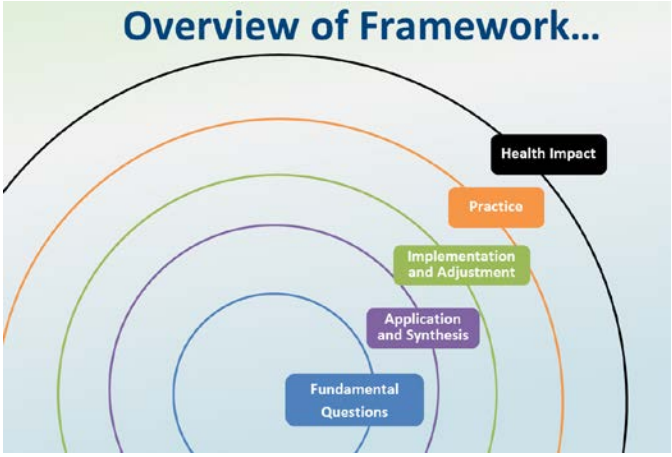
## Proposed Translational Framework for Environmental Health Sciences

### Overview

Many translational research frameworks consist of nodes that describe research somewhere along the basic, applied, clinical and public health trajectory, and links between those nodes (Trochim et al. 2011, Dougherty & Conway 2008, Westfall et al. 2007, Khoury et al. 2007, Sung et al. 2003). We used these models to inform our framework, but have incorporated three significant adaptations.

First, we propose to change the graphic representation from nodes/connections to a series of concentric circles (Figure 3). As with previous models, movement or bridging from one ring to the next is considered translational research. The rings represent the major translational research functions (i.e. the nodes or components that are typically labeled T1, T2, etc.).

**Figure 3. Overview of Translational Research Framework**




Second, we include descriptions of the types of activities that might occur within a particular ring. This level of detail (Figures 4, 6, 7, 8, 9, 10) allows researchers to tailor the model to tell a specific translational research story. Most importantly, we propose that this structure enables us to give "credit" to research that moves around the ring, in addition to research that moves from ring to ring.

Third, in order to capture more granularity in what has previously been termed the basic science area, we propose a Fundamental Questions ring that incorporates three concepts: research drivers or questions, experimental setting, and organism. By doing this we have created a framework that gives credit to fundamental science advances that are required for making major health advances.

Below we describe each ring of the framework. For simplicity sake, we start from the center ring and describe each ring as we move towards the outer ring, however we are fully aware that a translational research story may start on any ring, may skip rings and is likely non-linear.

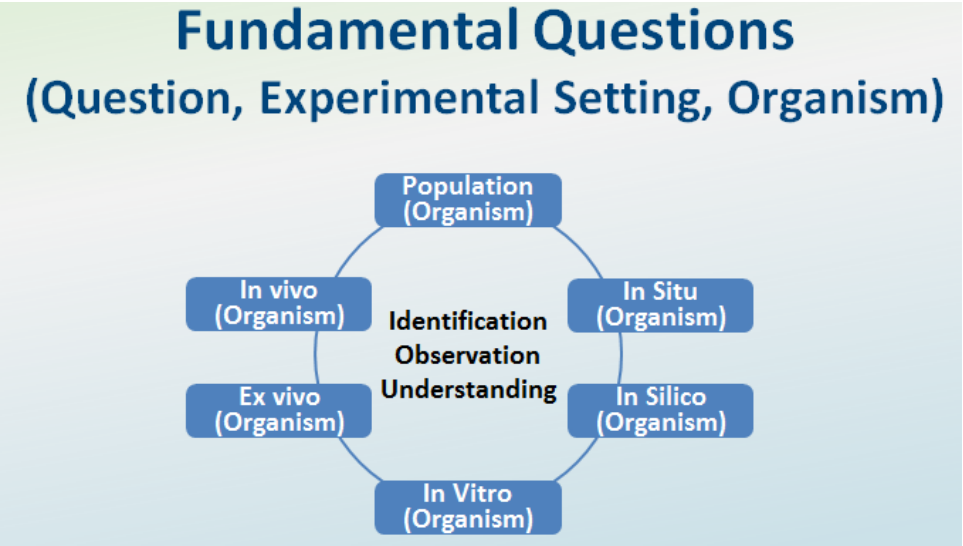
## Fundamental Questions

We created a Fundamental Questions ring to enhance the characterization of "basic" research (Figure 4). In working with examples, we found that the "basic" research questions we support fall into three major categories:

- Identification: What is it?
- Observation: What is it doing?
- Understanding: How does it do that and what else is going on?

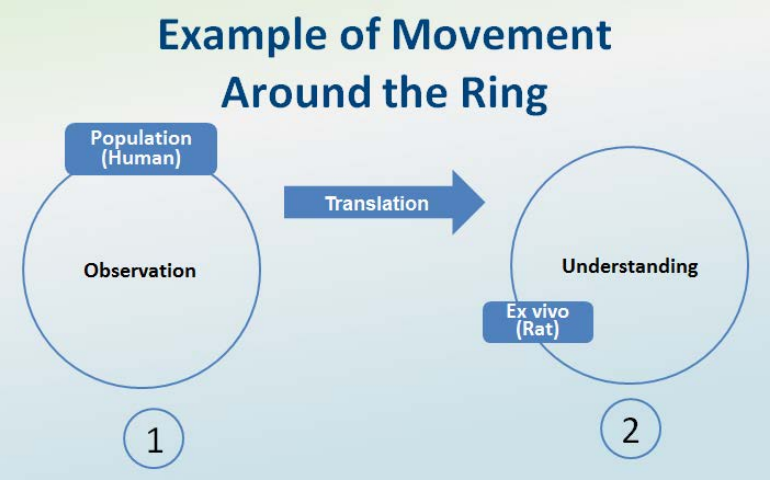
We place those categories at the center of the model and connect these questions with an associated experimental setting (*in vivo*, *in vitro*, *in situ*, *in silica*, or in a population at large), AND organism (human, animal, plant, bacteria, yeast, *c.ellegans*, other model organisms, etc.). We suggest that these three elements are intrinsically linked, and moving from one category to another represents important translational research.

**Figure 4. Fundamental Questions Ring**




For example, if a translational research story starts with an observation from an epidemiological cohort study (observation/population/human) and then moves to a lab-based study designed to discover a mechanistic understanding of the effect of an environmental exposure on a particular mouse model (understanding/ex vivo/mouse), then using our framework, the research would get credit for a translational bridge (Figure 5).

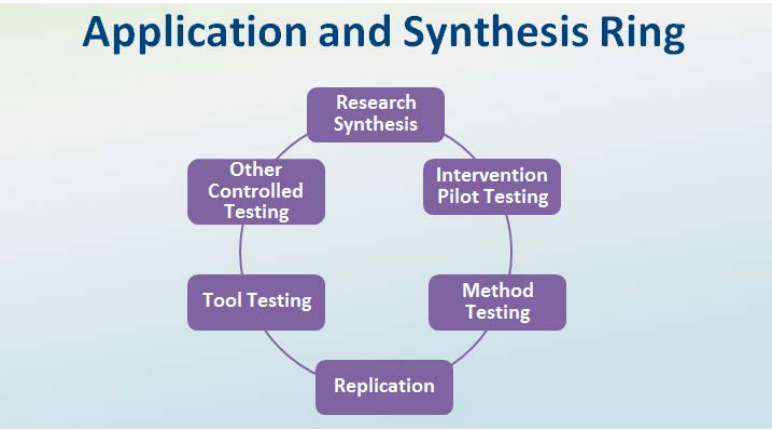
**Figure 5. Movement Around a Translational Ring**




## Application and Synthesis

The remaining rings have close parallels to a more traditional translational approach. At the application and synthesis ring researchers conduct experiments in a structured and predictable setting to gain deeper understanding of a process or a particular effect (Figure 6). Such activities could include pilot tests of interventions, methods/approaches, new tools (e.g. exposure sensors) or other highly controlled settings. Also on this ring is formal synthesis of previous research to inform future research, risk assessment, and other decision making.

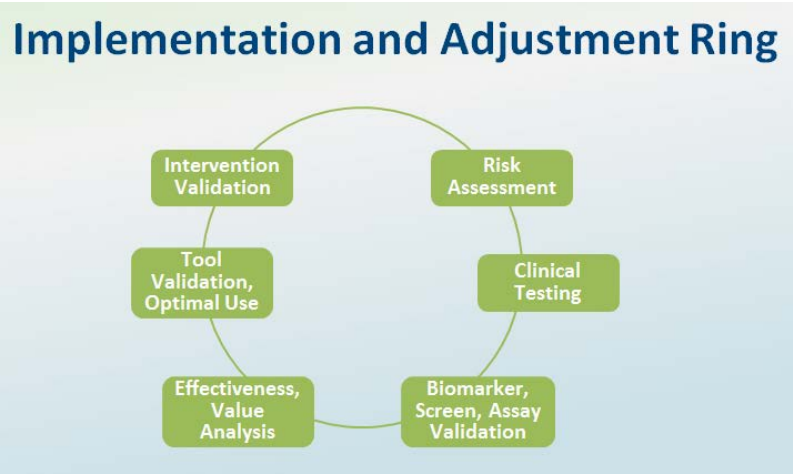
**Figure 6. Application and Synthesis Ring**



## Implementation and Adjustment

The next ring is about implementing hypotheses in real world settings and adjusting the product (intervention, tool, method, treatment, etc.) to account for differences in different settings and populations (Figure 7). Examples include biomarker, screen, or assay validation, clinical testing, tool validation and use, and effectiveness testing. This framework can also be linked to the field of dissemination and implementation research here (Glasgow et al 2012, Tabak et al. 2012, Majdzadeh et al. 2008, Davis et al. 2007, Landry et al. 2001, Wandersman et al. 2008, Huberman 1994, CIHR).

**Figure 7. Implementation and Adjustment Ring**




## Practice

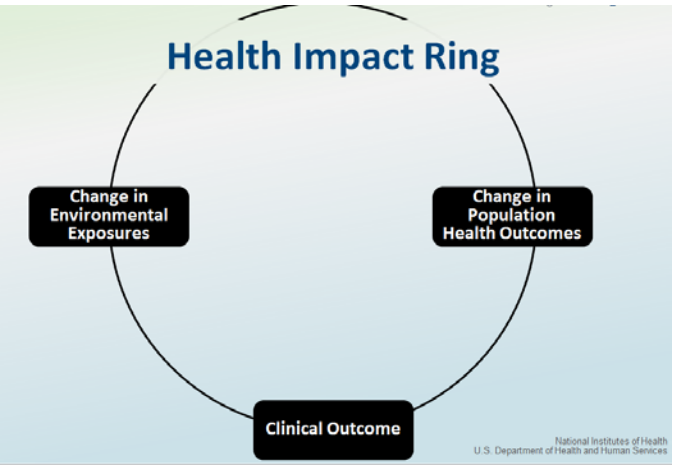
The next ring focuses on moving established ideas into common practice (Figure 8). This can include using evidence to inform new clinical guidelines, formalizing public health practice interventions, institutionalizing practices in local, regional, state, national or international policy, or motivating behavior change at an individual, family, community or population level.

**Figure 8. Practice Ring**

## Health Impact

The outermost ring addresses health impacts, in which we assess the broader environmental, clinical, or public health impact of a particular practice, guideline or policy (Figure 9). For example, if a state implemented a policy to reduce air pollution researchers might want to continue their research to assess the impact of the policy on air quality and related human health outcomes such as lung function or asthma rates.

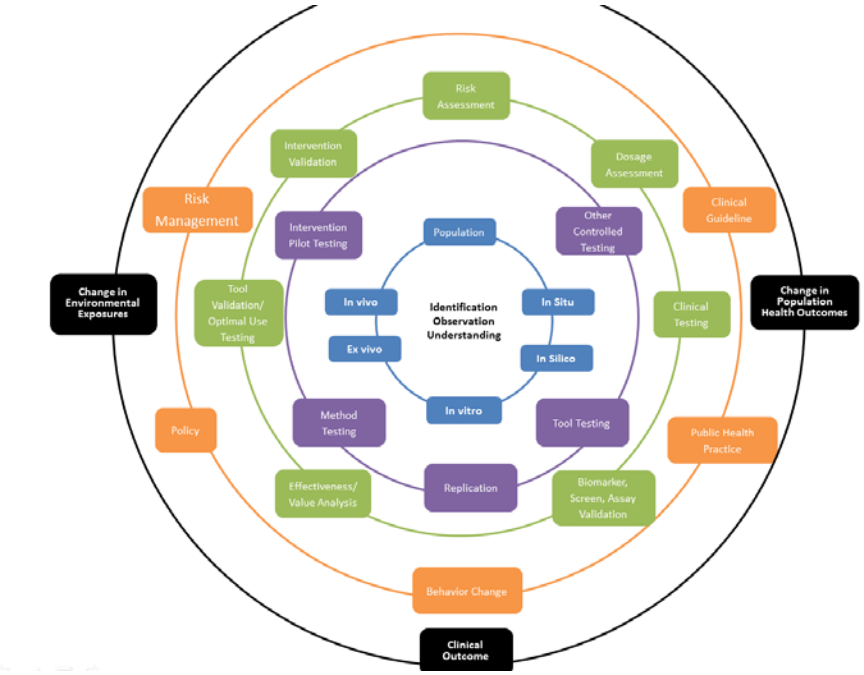
**Figure 9. Health Impact Ring**




## Full Framework

When all the rings are put together, the model highlights the complexity inherent in translational research (Figure 10).

**Figure 10. Full Translational Research Framework**



The proposed framework is intended to provide a clear concept of what NIEHS considers to be translational research. The framework provides general guidance about how scientific research might move back and forth within the framework over time to impact human health. However, we recognize that there are many more elements to the translational research story that are not reflected in the framework. We envision that this framework will serve as a common structure for a translational research story, but that other components of the story can be added as neededWe expect that public health policy or clinical guidelines are based on sound fundamental research and a series of testing and validation processes. Therefore, we have arranged the rings to reflect the general scientific process. However, a translational story can start at any point in the framework, can move in any direction and does not have to move linearly through all the rings. In fact, it may be common for research to "skip" a ring or two. It is also likely that research that moves to the outer rings will be supported by agencies other than NIEHS.

If the translational research story includes a fundamental question component, the story should include three elements as part of the description: the question or driver; the experimental setting; and the organism. While any project might be considered translational if it includes research that moves around a ring or from ring to ring, we expect that there will be degrees of translation, so that more complex or long-term translational stories will include more bridges.

## Case Studies

In this section, we show a proof of concept of how this framework can be used to tell a specific translational research story. This case study is included here as a means to illustrate different aspects of the framework and only represents a few key translational research milestones from the story. Further details about this story and other examples of translational research stories can be found at (http://partners.niehs.nih.gov/trf). A total of 7 detailed case studies have been developed at the time the RFA was released. Additional case studies may be added throughout the summer and fall.

We have also included a translational research template that allows reviewers to use the framework as a story telling tool. Additional components of the story could include the timeframe, descriptions of the people involved (specific individuals, groups or categories of people), descriptions of the labs, organizations or institutions involved, descriptions of moments of serendipity.

**Select Translational Research Milestones from an NIEHS Breast Cancer and the Environment Research Program (BCERP) from the University of Cincinnati regarding PFCs (UC PFC Example)**

- 2005 BCERP pilot project added polyfluoroalkyl chemicals (PFCs) to University of Cincinnati study based on findings from the Centers for Disease Control and Prevention NHANES (Calafat et al. 2005; Hiatt et al. 2007) (Figure 11)
- About half the Cincinnati girls assessed between 2005-2006 had serum concentrations >95th percentile (Pinney et al. 2014) (Figure 12)
- Haslam lab at Michigan State University found a stunting of mammary development and delayed onset of puberty in female mice exposed to PFCs. (Zhao et al, 2010) (Figure 13)
- University of Cincinnati researchers partnered with Cincinnati and Northern Kentucky water treatment departments between 2007-2012 to reduce exposure through water filtering (Grantee Communication with Program Officer) (Figure 14)
- All milestones on one slide (Figure 15)

**Figure 11. UC PFC Example Translational Milestone 1**

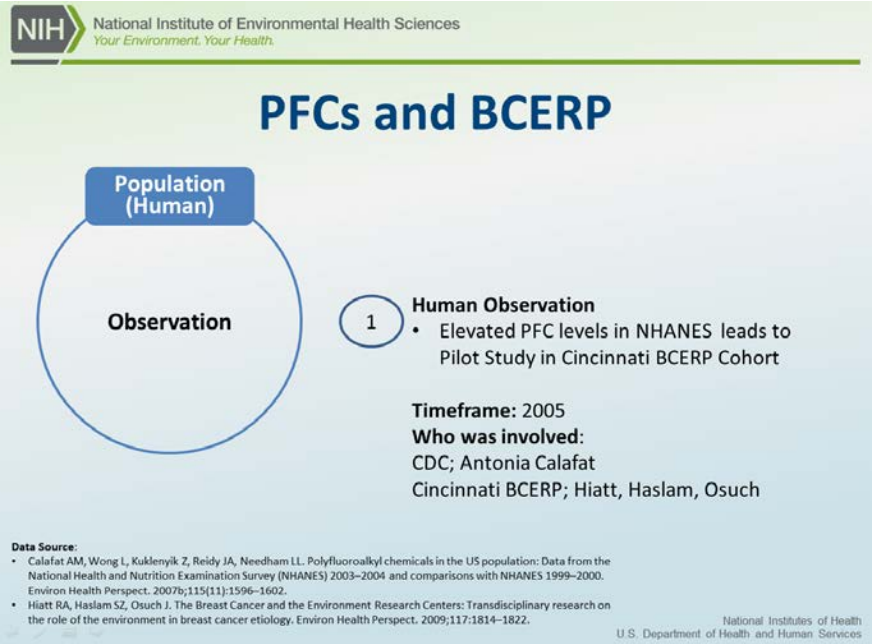



**Figure 12. UC PFC Example Translational Milestone 2**

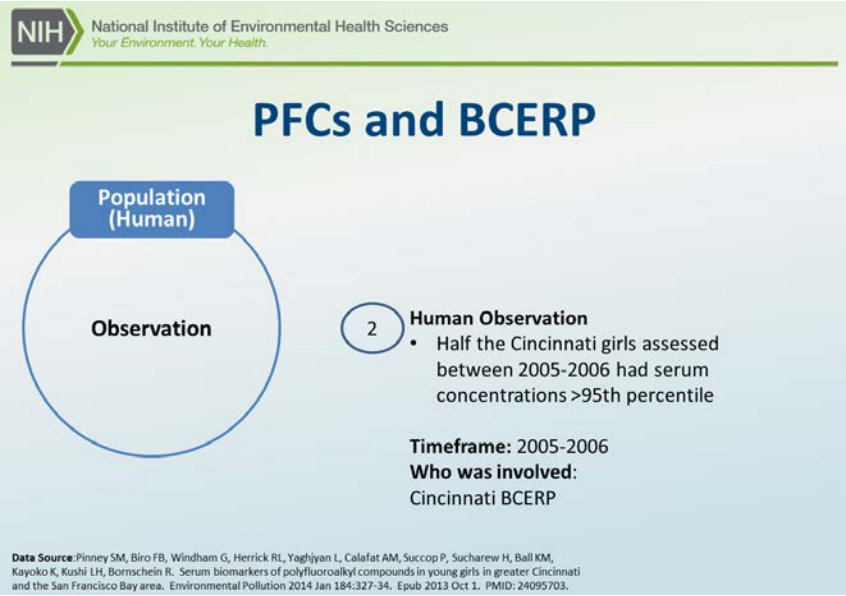


**Figure 13. UC PFC Example Translational Milestone 3**

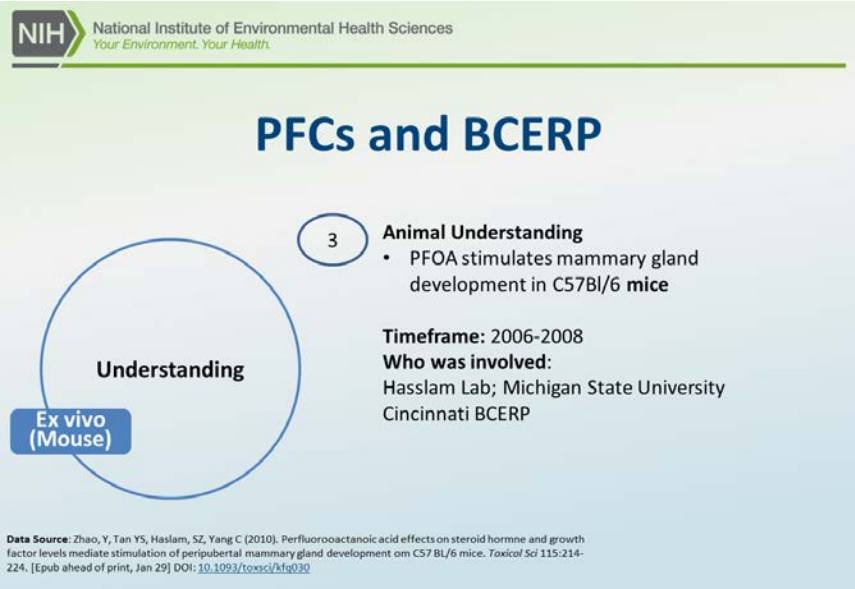
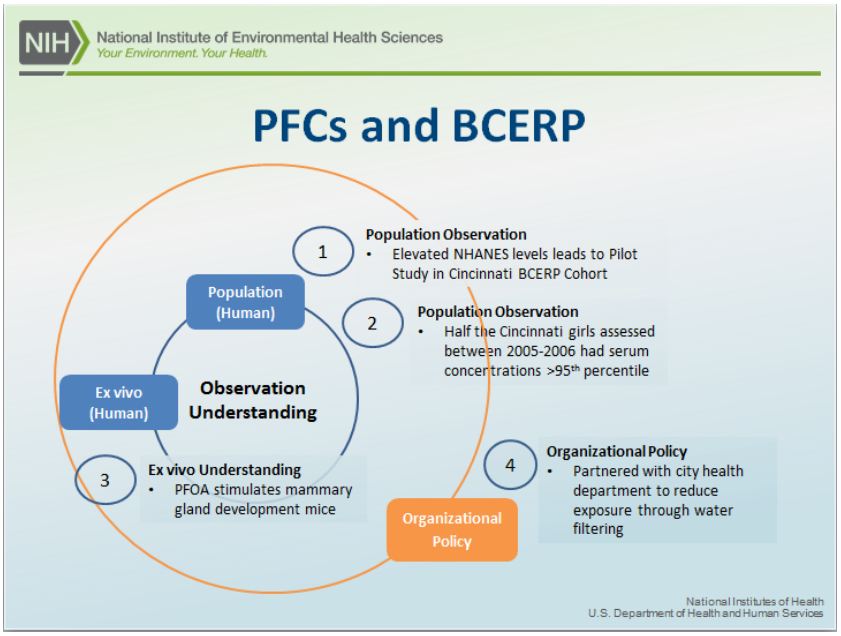



**Figure 14. UC PFC Example Translational Milestone 4**

**Figure 15. Combined Milestones**




## Limitations

As we present this model for broader comment. We encourage readers to keep the following caveats in mind.

First, as many modelers are quick to say, "All models are false. Some models are useful." This adage is a good reminder that we are not trying to create a perfect representation of translational research – or try to represent every aspect of the research res support. It is our hope, however, that this model brings us closer to being able to describe, compare and measure the translational research that we support at NIEHS.

Not all research is or will be translational. We do not expect every project to be plotted on this kind of framework. But to the extent that our researchers have translational research stories to tell, we believe this framework can help provide a common vocabulary and sign posts.

Research translation is the dissemination of research findings to many different kinds of communities. NIEHS appreciates and values research translation and community based research, but other frameworks describe those processes and so they are not explicitly included in this model. We do anticipate that contributions of community partners will easily be reflected in descriptions of the translational research and in the recognition of collaborators in the process (see the detailed examples for illustrations of this concept).

## Anticipated Benefits of Revised Translational Research Framework

Developing and communicating a clear concept of translational research helps reinforce the NIEHS strategic plan (http://www.niehs.nih.gov/about/strategicplan/) for the institute and helps ensure that grantees, program staff and institute leadership are all working from a common understanding of translational research. The translational research framework also provides a storytelling structure that will enable researchers to clearly articulate the complex, multi-year (or even multi-decade) process of translational research. In the Core Centers evaluation we yearned for a way to move beyond static "snapshots" of research descriptions and move toward a more animated "movie". The framework proposed is largely designed to describe the translational process in a more animated way.

The framework will enable us to better assess where a given research project falls along the translational research spectrum, provide a mechanism to categorize and understand current status of the portfolio, and enable us to track movement of research through translational spectrum. As an evaluation tool, the framework will enable us to code research projects using these modified categories to give more "credit" to research that moves through several iterations in the basic science area.

Finally, the framework will enable us to talk more clearly about the bridging between areas of the translational research framework. As science managers, the framework will allow our NIEHS staff to actively engage in bridging science between areas of the translational research framework. Similarly, the framework can provide researchers with a map of potential paths that their research might take through the translational research cycle. The framework can also be used to identify gaps and to think about potential collaborators that could be included to help bridge these gaps.

## Comments welcome!

We welcome your input on the framework. This draft and the associated examples will be available for comment until October 15, 2016. Please provide your comments by using the online form available at https://www.research.net/r/trf2016_survey.

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