Applying Translational Science Approaches to Protect Workers Exposed to Nanomaterials

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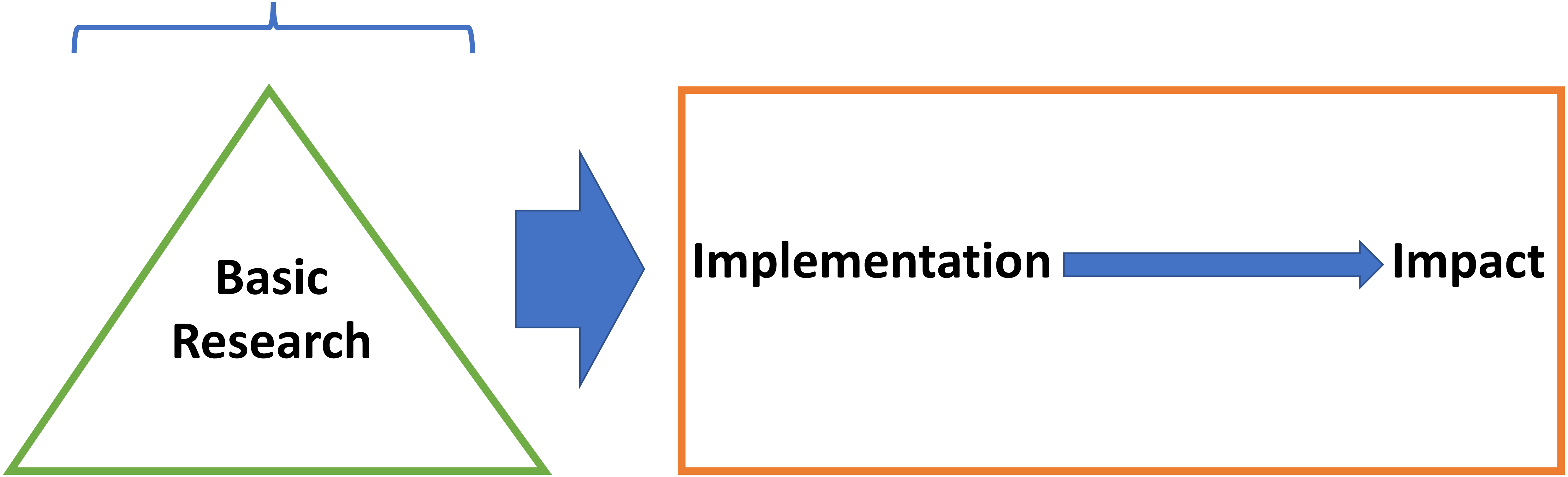
The occupational safety and health (OSH) field has historically focused on the etiologic end of the research-to-practice continuum rather than the dissemination, implementation and public health impact end.

Historic Focus of Occupational Safety and Health Field



There has been a call to increase efforts to investigate factors that limit or **enhance**

- Development
- Transfer
- Use

Of OSH risk factor and intervention information and technology

Thus ensuring that this knowledge leads to improvements in workers' health

Translational Science

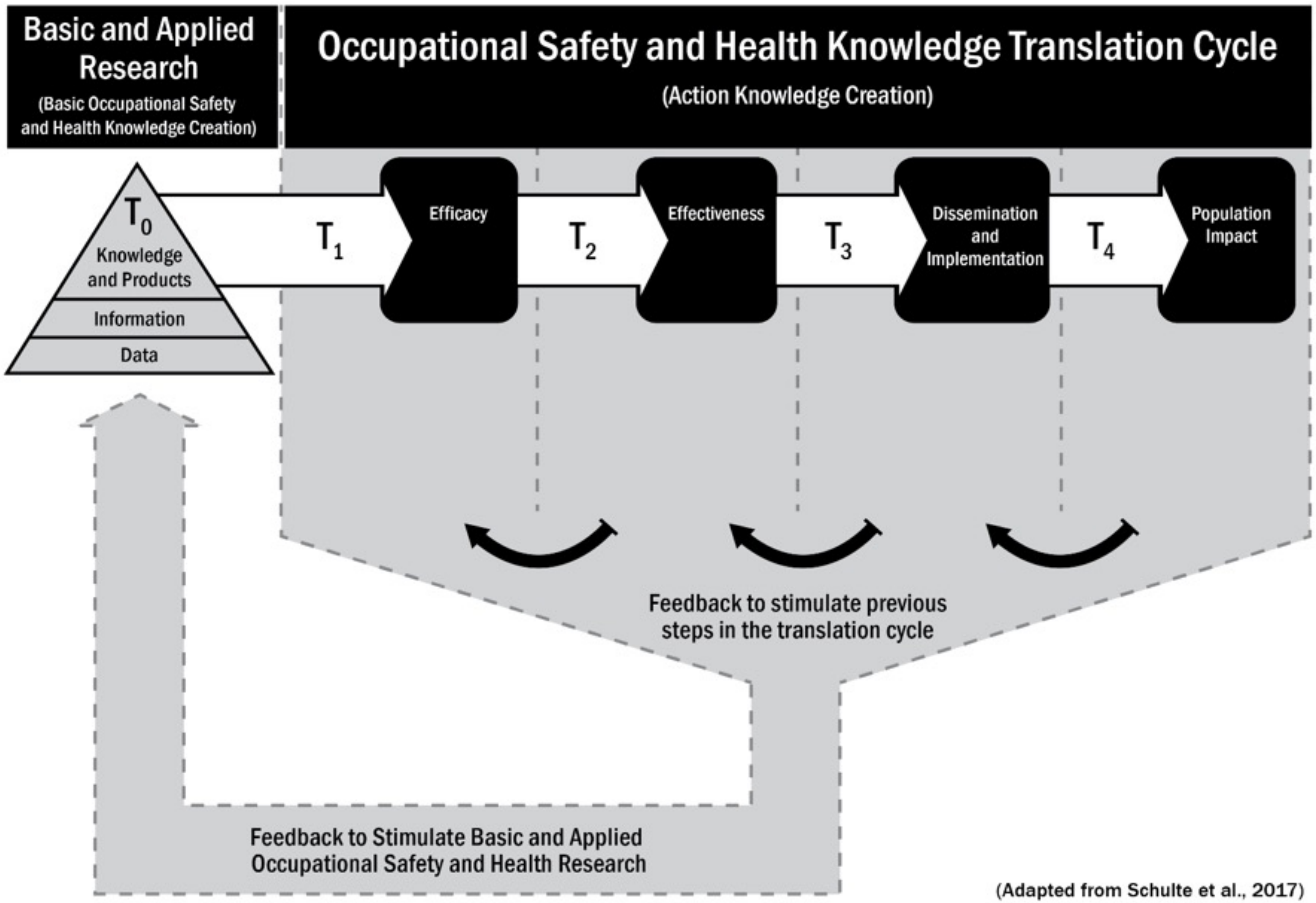
"…the application of scientific investigative approaches to study how the outputs of basic and applied research can be effectively translated into practice and have an impact." (Schulte et al., 2011)

"…comprehensive applied research that strives to translate the available knowledge and make it useful."

(Narayan et al., 2000)

"…research steps to take scientific discoveries 'from the bench to the beside and back again.'" (Fort et al., 2017)

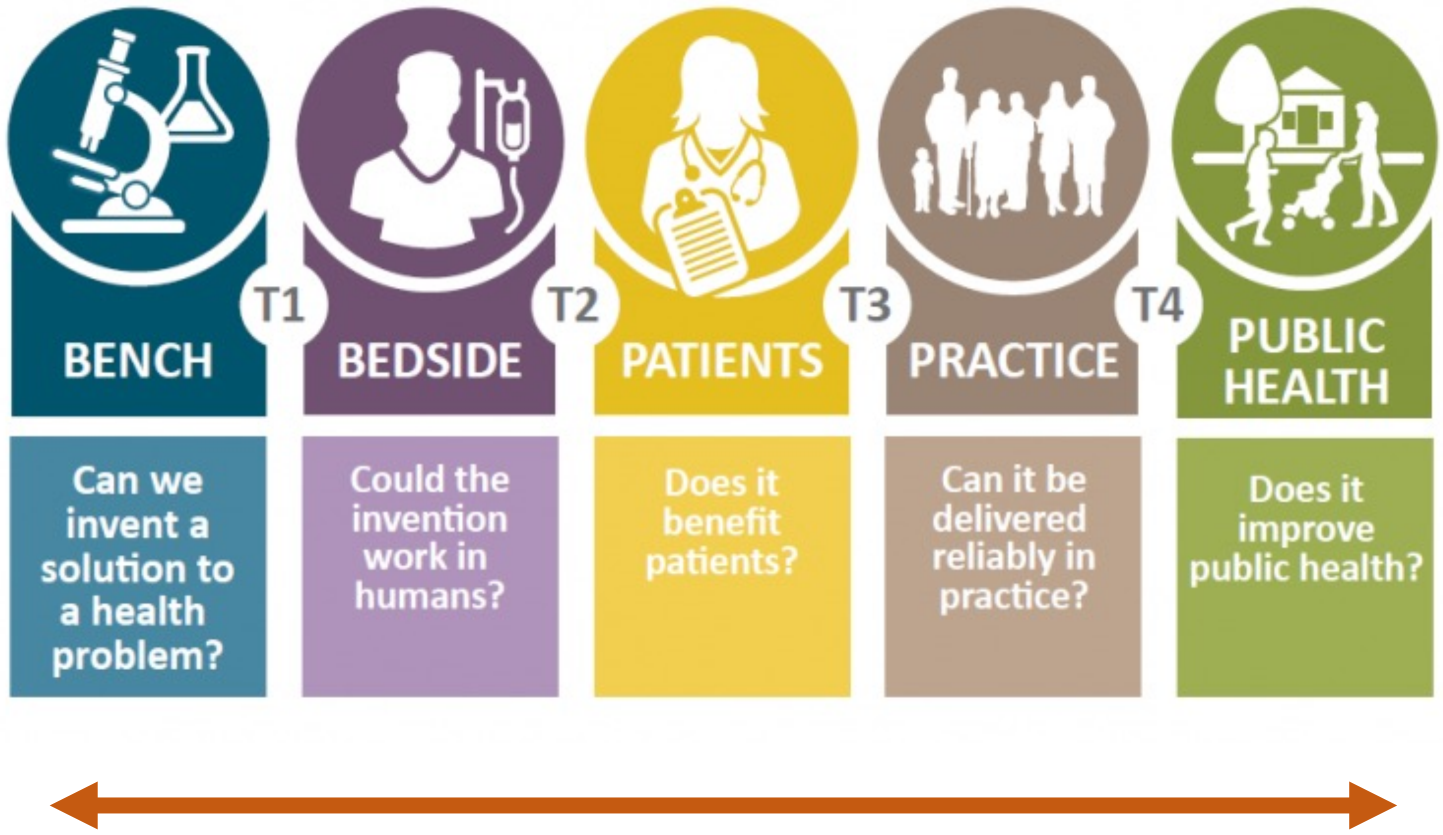
Figure 1. Overview of Translational Science for Occupational Safety and Health



(Adapted from Schulte et al., 2017)

Translational science in OSH builds on

- NIH model (2003) and interpretation by Khoury et al. (2004)
  - “Bench-to-bedside”
  - 4 phases: T1-T4
  - Characterized by moving findings to a larger scale
  - Focuses on how best to make those transitions
  - Also builds on:
    - Westfall, Mold, & Fagnan (2007).
    - Public health model of Ogilvie et al. (2009)
    - Knowledge to Action (Graham et al. 2006; Wilson et al. 2011)
    - Knowledge Transfer and Exchange (Lavic et al. 2003; Van Eerd et al. 2011)
    - Application by Lucas et al. (2014)



BENCH
T1
BEDSIDE
T2
PATIENTS
T3
PRACTICE
T4
PUBLIC HEALTH
Can we invent a solution to a health problem?
Could the invention work in humans?
Does it benefit patients?
Can it be delivered reliably in practice?
Does it improve public health?

Translational Research is **not:**

- r2p (research to practice)
- Translation

Rather it is the study of these activities

Phase 1: Efficacy Research

- Study of the efficacy of an intervention or information that could be used to protect workers.

Examples of interventions to address worker exposure to ENMs

Intervention	Example
Program	OECD Characterization
Practices	Occupational Exposure Limits
Principle	Consider ENM hazardous until proven otherwise
Procedures	Nanomaterial Exposure Assessment Technique
Products	Direct reading instrumentation
Policies	ISO/TC 229 Nanotechnologies voluntary standards, WHO guidelines on protecting workers from potential risks of manufactured nanomaterials.

Adapted from Brown et al., 2017

Phase 2: Effectiveness Research

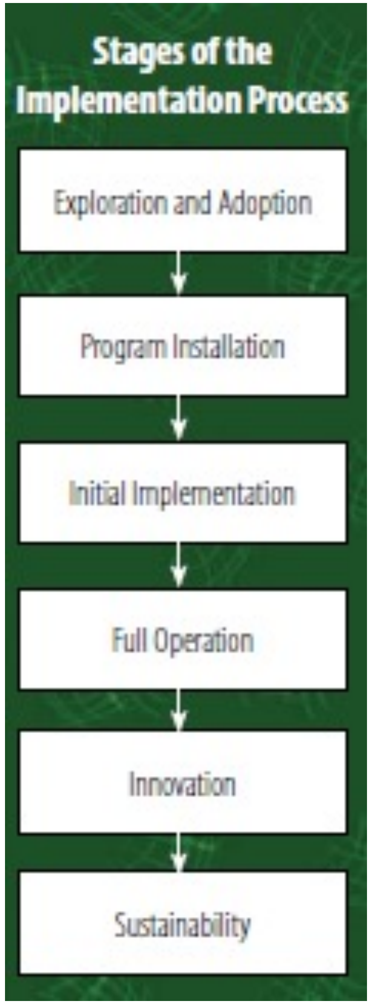
- Assess effectiveness of a new recommendation or intervention in real-world settings to develop generalizable knowledge

Phase 3: Dissemination and Implementation Research

- Study the movement of evidence-based technology and interventions into well accepted OSH practice
- Identify barriers and facilitators to implementation, dissemination
- Engage key stakeholders (throughout all translational stages)
- Focus on occupational health equity
- Consider and characterize the multi-level context and environment
- Identify implementation strategies and mechanisms of action

Implementation Science

Implementation Science is the study of factors that influence the full and effective use of innovations in practice. The goal is not to answer factual questions about what it is, but rather to determine what is required (National Implementation Research Network).



(Fixsen et al. 2005)

D&I Theories, Models and Framework (TMFs)

- Tools to guide the development and evaluation of D&I studies
- More than 150 have been identified
- Commonly used ones:
  - Consolidated Framework for Implementation Research (CFIR; Damschroder et al., 2009),
  - RE-AIM (Reach, Effectiveness, Adoption, Implementation, Maintenance) framework (Glasgow et al., 1999; Glasgow et al., 2019)
  - EPIS (Exploration, Planning, Implementation, Sustainment) framework (Aarons et al., 2011)
  - Diffusion of Innovation theory (Rogers, 2003)
  - Theoretical Domains Framework (TDF) (Michie et al., 2005).

Study designs used in D&I research

- Experimental (e.g., randomized controlled trial, cluster-randomized controlled trial, pragmatic trial, stepped wedge trial, dynamic wait-listed control trial)
- Quasi-experimental (e.g., nonequivalent groups, pre-/post-, regression discontinuity, interrupted time series)
- Nonexperimental or observational (including designs from epidemiology)
- Mixed-methods (i.e., the collection and integration of qualitative and quantitative)
- Qualitative methods (e.g., focus groups, semistructured interviews)
- System Science approaches (e.g., system dynamics, agent-based modeling)

(Gila et al. 2018)

Phase 4: Population Impact Research

- Investigate large-scale use of interventions and their impact

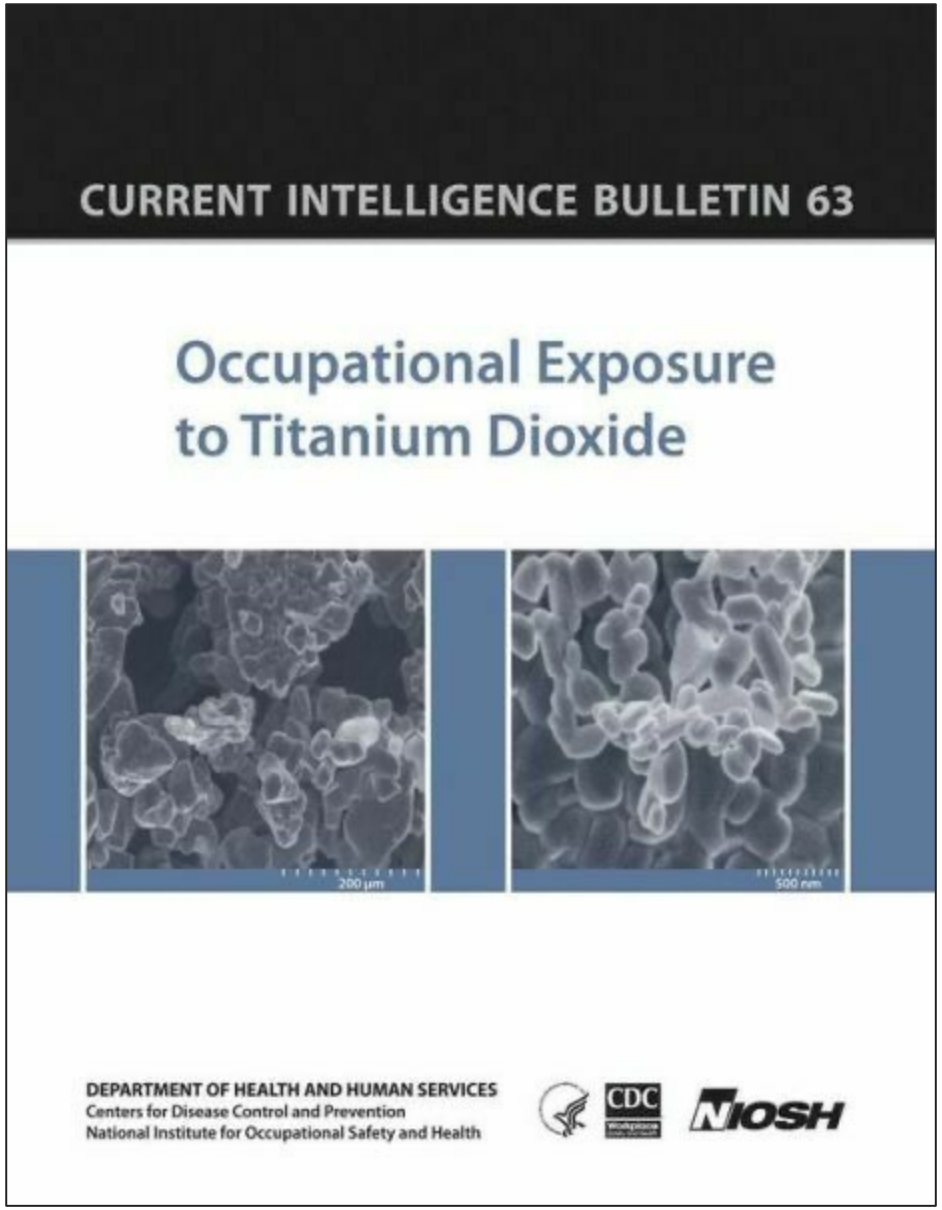
Three examples to assess for translational research in nanotechnology

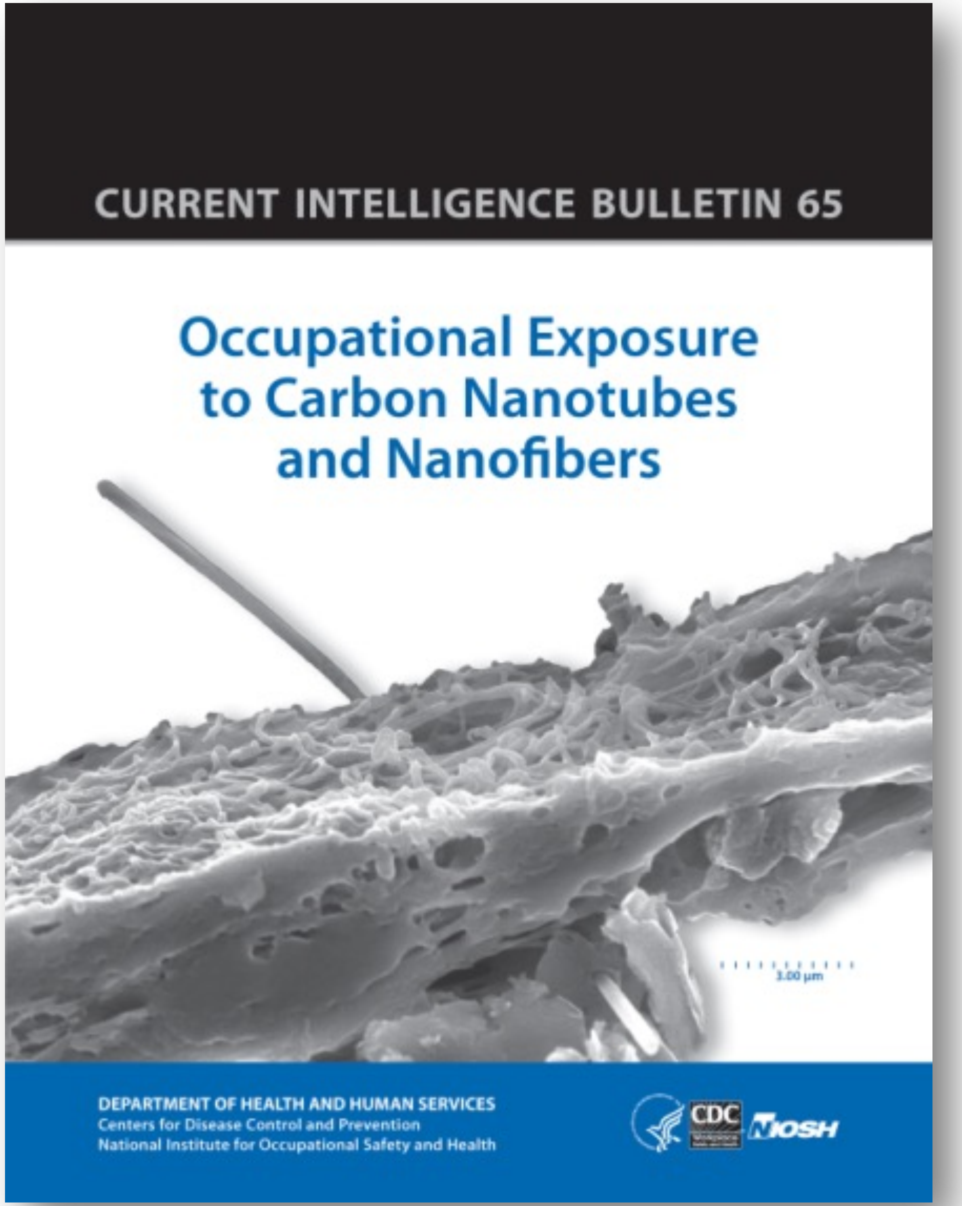
- NIOSH recommended exposure limits for Titanium Dioxide and Carbon Nanotubes/Nanofibers

- WHO Guidelines On Protecting Workers from Potential Risks of Manufactured Nanomaterials

- International Risk Governance Council (IRGC) White Paper on Nanotechnology Risk Governance

Example 1. NIOSH Recommended exposure limits for TiO_2 and CNT/CNF


CURRENT INTELLIGENCE BULLETIN 63
Occupational Exposure
to Titanium Dioxide
DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health
CDC
NIOSH


CURRENT INTELLIGENCE BULLETIN 65
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National Institute for Occupational Safety and Health
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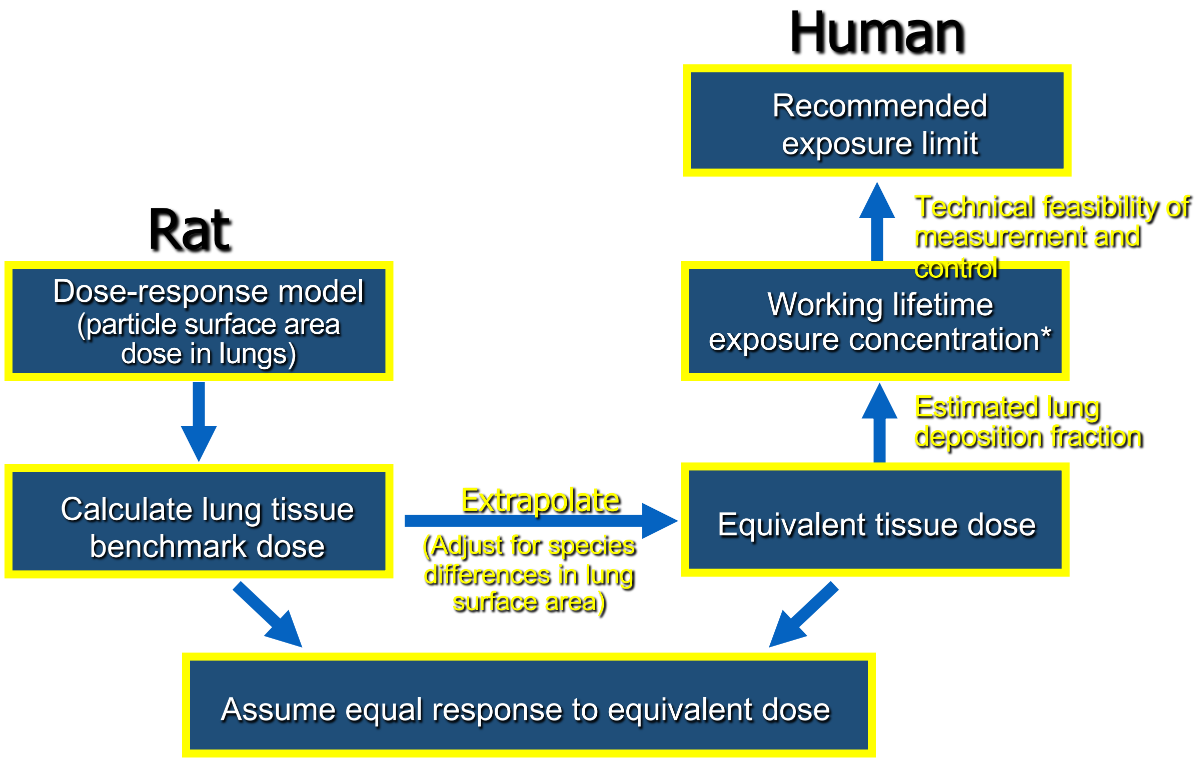
NIOSH

Quantitative Risk Assessment in Developing Recommended Exposure Limits for Nanoparticles



*Compare rat-based risk estimates with confidence intervals from human studies

Ultrafine (Nanoscale) TiO_2

- Recommended Exposure Limit
  - 0.3 mg/m^3 (TWA for up to 10 hrs/day for a working lifetime)
  - Estimated to reduce risk of lung cancer below 1 in 1,000

Risk Assessment: Carbon Nanotubes

- Used data from Ma-Hock (2009)
  - Wistar rats exposed by inhalation to 0.1, 0.5, 2.5 mg/m^3 multiwall carbon nanotubes (6 hr/day, 5 days/wk, 15 wks)
- Recommended Exposure Limit (REL) for respirable CNT/CNF 1 μg/m^3 (as elemental carbon) as an 8-hr TWA.
- Reduce risk of pulmonary fibrosis and acute pulmonary inflammation.

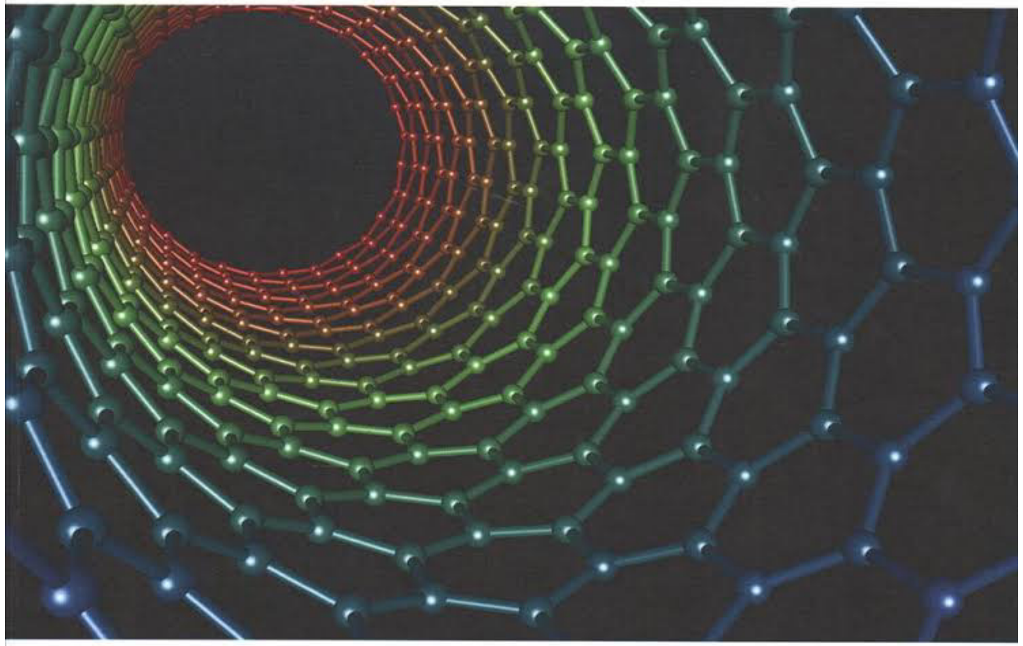
Translation Science

Example 1: Recommended Exposure Limits (TiO_2 & CNT/CNF)[1,2]		
T_0	Basic Science	• Ultrafine and fiber toxicity • Specific studies of ENMs • Quantitative risk assessment
T_1	Efficacy	• Sensitivity analysis of risk assessment • Historical basis for OELs
T_2	Effectiveness	• No examples • Extensive use
T_3	Dissemination & Implementation	• No examples • Hypothetical questions
T_4	Population Impact	• Use of intermediate indicators (e.g., Iavicoli et al. 2020) • Longitudinal studies • Sustainability studies

1. NIOSH 2011
2. NIOSH 2013

Example 2. WHO Guidelines on Protecting Workers from Potential Risks of Manufactured Nanomaterials

WHO GUIDELINES ON PROTECTING WORKERS FROM POTENTIAL RISKS OF MANUFACTURED NANOMATERIALS



World Health Organization

WHO Recommendations

6.1 Assess health hazards of manufactured nanomaterials (MNMs)

6.2 Assess exposures to MNMs

6.3 Control exposure to MNMs

6.4 Health surveillance

6.5 Training and involvement of workers

Translation Science

Example 2: WHO Guidelines for protecting workers		
T_0	Basic Science	• Historic and contemporary toxicity data • Stakeholder requests
T_1	Efficacy	• PICO analysis (Population, Intervention, Comparison group, Outcome) • International expert assessment
T_2	Effectiveness	• Historical practice • No studies • Cross-sectional and prospective studies
T_3	Dissemination & Implementation	• Implementation plan • No D&I research
T_4	Population Impact	• No population data • Use of intermediate indicators • Longitudinal studies

1. WHO 2017

Example 3. IRGC White Paper on Nanotechnology Risk Governance

irgc

white paper on

RISK GOVERNANCE

TOWARDS AN INTEGRATIVE APPROACH

international risk governance council

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2006

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Perspectives

Nanotechnology and the need for risk governance

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Abstract

After identifying the main characteristics and prospects of nanotechnology as an emerging technology, the paper presents the general risks associated with nanotechnology applications and the deficits of the risk governance process today, concluding with recommendations to governments, industry, international organizations and other stakeholders. The International Risk Governance Council (IRGC) has identified a governance gap between the requirements pertaining to the nano- rather the micro-/macro- technologies. The novel attributes of nanotechnology demand different routes for risk-benefit assessment and risk management, and at present, nanotechnology innovation proceeds ahead of the policy and regulatory environment. In the shorter term, the governance gap is significant for those passive nanostructures that currently in production and have high exposure rates ; and is especially significant for the several 'active' nanoscale structures and nanosystems that we can expect to be on the market in the near future. Active nanoscale structures and nanosystems have the potential to affect not only human health and the environment but also aspects of social lifestyle, human identity and cultural values. The main recommendations of the report deal with selected higher risk nanotechnology applications, short- and long-term issues, and global models for nanotechnology governance.

Background

Defining Nanotechnology

Nanotechnology is still in an early phase of development, and is sometimes compared in the literature to information technology in the 1960's and biotechnology in the 1980's. Nanotechnology refers to the development and application of materials, devices and systems with fundamentally new properties and functions because of their structures in the range of about 1-100 nanometres (Siegel et al., 1999). It involves the manipulation and/or creation of material structures at the nanoscale, in the atomic, molecular supramolecular realm. At the nanoscale, the characteristics of matter can be significantly changed, particularly under 10-20 nm, because of properties such as the dominance of quantum effects, confinement effects, molecular recognition, and an increase in relative surface area. Downsized material structures of the same chemical elements change their mechanical, optical, magnetic and electronic properties,

IRGC Nanotechnology Risk Policy Recommendations

- Improve the knowledge base
- Standardise nomenclature measuring and handling systems
- Better understanding of risk
- Improve data sharing
- Understand the full implications
- Strengthen risk management structures and processes
- Identify gaps and remedies
- Development of Voluntary systems
- Need to consider anticipatory and coordinated measures for possible events where nano-technology based applications would produce irreversible and significant damage
- Promote stakeholder communication and participation
- Distinguish between passive and active nanomaterials and products
- Improve communication strategies
- Engage the public and make participation count
- Ensure broad social benefits and acceptance
- Stakeholder participation in setting priorities
- Funding for the public good
- Reduce barriers for developing countries
- Economic planning to reduce adverse impacts
- Collaboration between stakeholders and nations

(IRGC 2006)

Translation Science

Example 3: International Risk Governance Council guidance on nanotechnology		
T_0	Basic Science	• Historic and contemporary toxicity data • Explosiveness data • Stakeholder request
T_1	Efficacy	• Scoping review on deficit in guidance
T_2	Effectiveness	• No studies • Synthesis of evidence for risk governance
T_3	Dissemination & Implementation	• No studies • Possible research: extent employers received guidance/best means of dissemination
T_4	Population Impact	• No studies • Longitudinal studies

1. IRGC 2006

Conclusions

- There are practically no examples of applied translation science to the ENM worker realm.

- There is a need for translation science to be applied to ENM workers' exposure

- If OSH research on ENMs is to lead to worker protection:
  - More focus on distal end of research-to-impact continuum
  - Increase collaboration with specialists in translational science
  - Increase funding of translational science
  - Utilize findings of translational science research to improve impact

Thank you!

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