

The long, perilous postdoc
Nextgen research independence
K99/R00: navigating the transition

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UCSF K99/R00 Workshop
May 17, 2018

Biomedical research at an inflection point



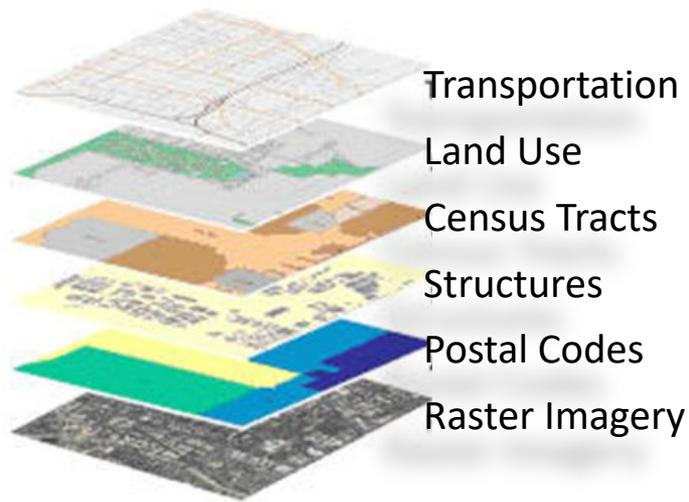
*data collection; detailed
description of biological
processes; traditional
education*

*mechanistic understanding of
biological processes; biological
solutions for big problems; “need
to know” education*

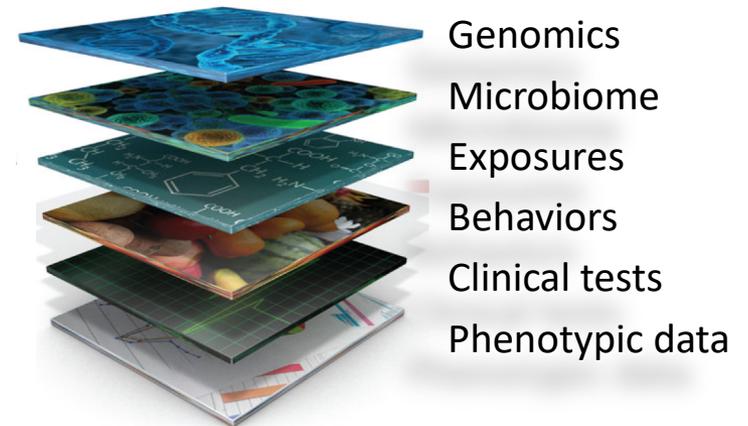
How move through the inflection point?

- *Merge sciences:* incorporate concepts and technologies of physical sciences, engineering, computing/AI, informatics
- *Build learning system:* computational knowledge network; continuum across basic discovery, tools and applications, health and health care, social issues in health, environment, energy, food
- *Rethink education, workforce, policy:* broad literacy with specialized expertise, team research, “research toolkit”, “night science”, informed career decisions, short training period

What if we had a knowledge network for biological information?



Google Maps



Knowledge Network

- Connections between layers integrate diverse data types, suggest lab-testable hypotheses, self-assemble diverse teams, define normal and disease mechanisms, drive clinical trials and drug development, inform health and care decisions

(Towards Precision Medicine: Building a Knowledge Network for Biomedical Research;
http://www.nap.edu/catalog.php?record_id=13284)

Knowledge network would drive transdisciplinary research

- Network connects data types, reveals correlations, patterns
- Network connects researchers, facilitates transdisciplinary teams
- Teams generate bold ideas and approaches
- Team composition is dynamic, driven by project needs
- Scalable: local, federal, multinational, trans-sector (.edu, .com, .org, .gov)
- Suggests model for “University of the Future”
(<http://assets1b.milkeninstitute.org/assets/PillarPage/POI/2016P4C/12YamamotoSingle-Page.pdf>)
 - *What do PhD and postdoc trainees need to know to advance in tomorrow's biomedical research ecosystem?*
 - *How well does today's education address that “need to know”?*
 - *In today's world, how navigate the transition to independence?*

Today's biomedical graduate and postdoc education

- Relatively static training process in a highly dynamic field
- Discipline-specific apprenticeship; cloning mentors
- Bold thinking/projects are actively discouraged by hypercompetitiveness, anxiety over funding and advancement
- Time to independence: 6-7 years to PhD; 4-5 year first postdoc; 10-15 years total
- Independence viewed as individual performance

We seem to have converted one of the more exciting, creative and rewarding human endeavors into a pedantic slog

It wasn't easy, but we did it!!

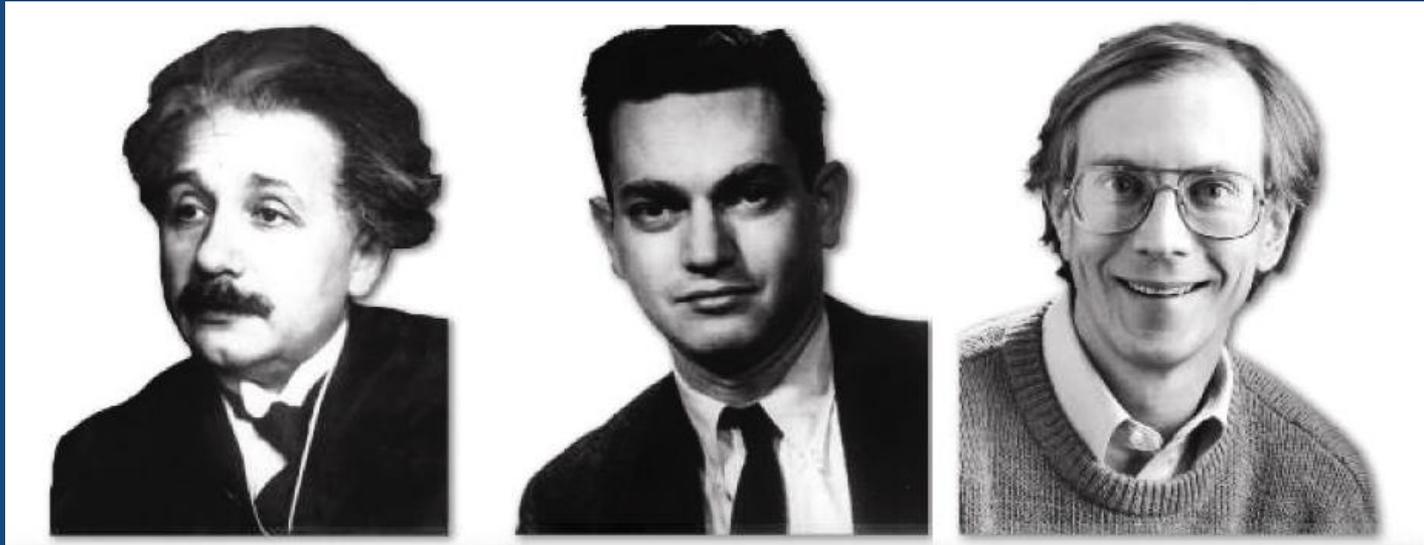
The Perilous, Slow Transition to Independence

- Median age, first independent position: 38
- Median age, first R01: 42
- Percent NIH awards to new investigators: 4

Even the most talented of our young people seem to be forced to endure several years of rejected grant applications before they finally acquire enough “preliminary data” to assure the reviewers. -- Bruce Alberts

It is not manageable...to have a culture where young investigators are discouraged from either entering a field, or...get discouraged about taking risks and bringing science into the new directions that it needs to go. --Elias Zerhouni

Losing some of the best years?



Albert Einstein

Marshall Nirenberg

Tom Cech

First Position: 32

33

31

Nobel Prize: 42

41

42

>> Need to train more efficiently: 4-8 years!

>> Need to support asking bold questions

Day science calls into play arguments that mesh like gears, results that have the force of certainty...
Conscious of its progress, proud of its past, sure of its future, day science advances in light and glory.

By contrast, night science wanders blind, it hesitates, stumbles, recoils, sweats, wakes with a start. Doubting everything, it is forever trying to find itself, question itself, pull itself back together.

Night science is a sort of workshop of the possible, where what will become the building material of science is worked out.

-Francois Jacob

If at first the idea is not absurd, then there is no hope for it.

-Albert Einstein

What do PhD students Need-to-Know for 21st century success?

- Specialized expertise embedded in broad literacy
- Acquire “Research toolbox”: [a] identify important problems; [b] execute experiments; [c] choose which results to pursue

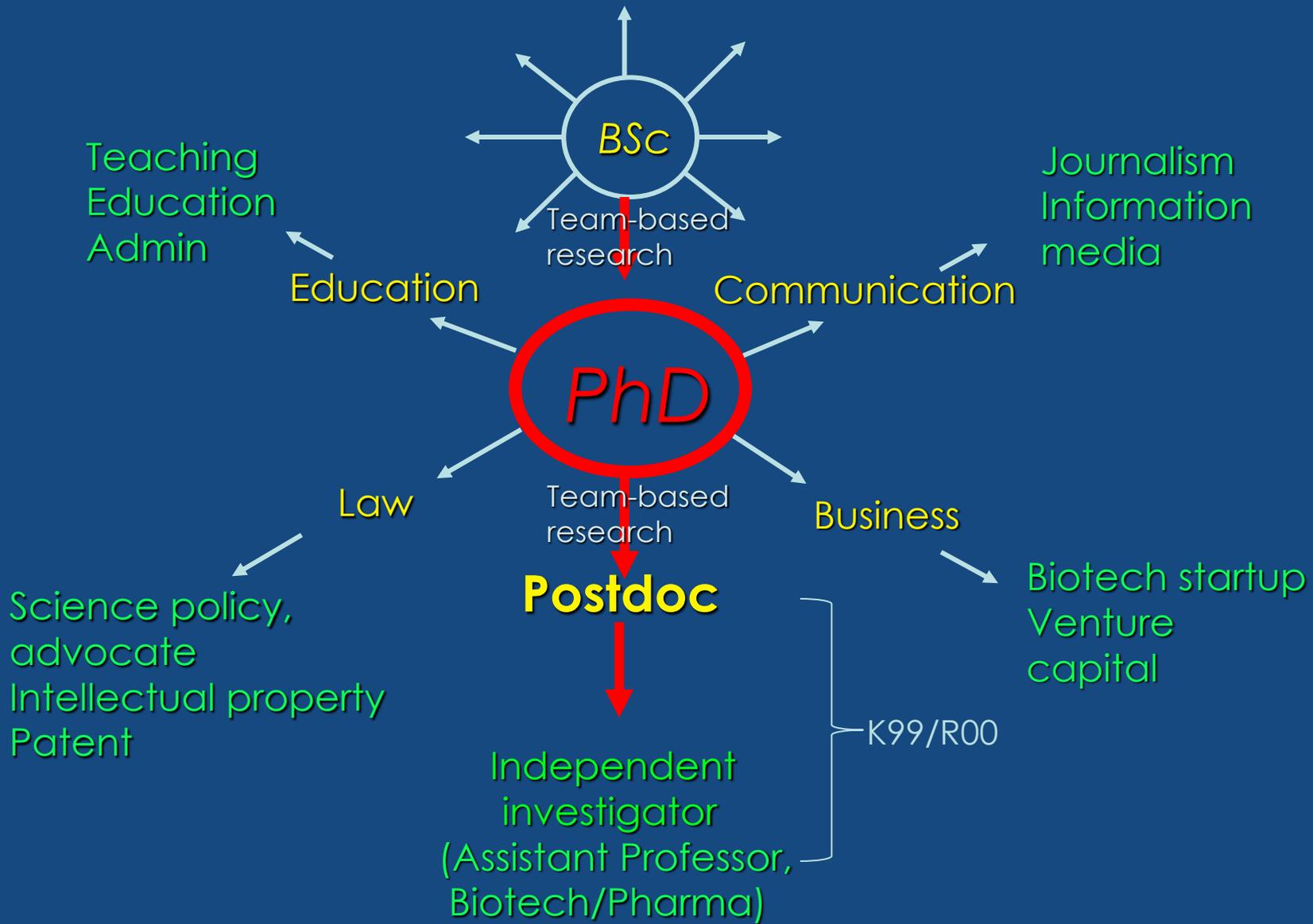
Experimental execution includes:

- *Conceptualization of approach*
- *Creation/adoption of best methods*
- *Quantitation, statistical significance*
- *Interpretation*
- *Publication*

- Mentored, original, ethical, exciting, team-based research
- Communicate impact to peers and public
- Working familiarity with career options

Consider what's not on the list

Goals: Team research, PhD “hub”, career option “spokes”



Missions and goals for PhD and postdoc education

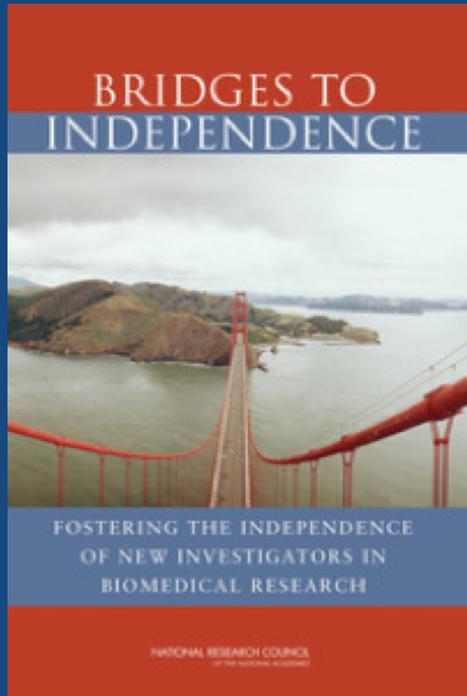
PhD students:

- Specialized expertise embedded in broad literacy
- “Research toolbox”: *[a] identify important problems; [b] design experiments; [c] choose which results to pursue*
- Mentored, exciting, original, ethical team-based research
- Communicate impact to peers and public
- Working familiarity with career options

Postdocs:

- Skills for the practice of science
- Skills for developing and managing independent research program *with support for the transition*

K99/R00 – Support for the postdoc-PI transition



2005 National Academy of Sciences (<http://nap.edu/11249>)

Independent investigator:

- Not defined as a researcher with an NIH R01 grant, or one who can work in isolation, or who is “self-sustaining” or “separately funded”

- Instead, a researcher “who enjoys independence of thought—the freedom to define the problem of interest and to choose or develop the best strategies and approaches to address that problem.”

One of 13 recommendations:

- NIH should establish a grant mechanism, available to U.S. citizens as well as non-citizens or permanent residents, to promote the conduct of innovative research by scientists transitioning into their first independent positions.

- These research grants should provide sufficient funding and resources for promising scientists to initiate an independent research program and allow for increased risk-taking during up to 2 *final* years of *mentored* postdoctoral training and up to 3 *initial* years of their *independent* research effort.

K99/R00 – NIH Pathway to Independence Award

o Provides postdoctoral scientists support for sequential mentored and independent research

- K99 phase: 1-2 years; <\$100k/yr salary + benefits, <\$30k/yr research support
- R00 phase: 1-3 years; <\$249k/yr salary, benefits, research, indirect costs
- Feb, Jun and Oct application deadlines; up to 5 years of total support

o Applicants must have <4 years of postdoctoral research experience at the time of the initial or the subsequent resubmission or revision application.

o Applicants achieving independence (*i.e.*, any faculty or non-mentored research position) before a K99 Award is made lose eligibility for K99 or R00 funding

o Applicants may be U.S. citizens or non-citizens. Visa status during each phase of the K99/R00 Award must allow the PI to conduct the proposed research at the applicant institution.

o The R00 Institution may not require the use of R00 funds to offset a typical start-up package (salary and other).

o The R00 Institution must provide assurance that the PI's appointment is not contingent on funding of the R00 Award to the institution.

K99/R00 – one mechanism, many flavors

PA-18-398: current “parent announcement” of the K99/R00 mechanism

BUT...

NIH is a loose federation of 27 independent Institutes and Centers (ICs)

“Special Note: Not all NIH Institutes and Centers participate in Parent Announcements. Applicants should carefully note which ICs participate in this announcement and view their respective areas of research interest and requirements at the Table of IC-Specific Information, Requirements and Staff Contacts website.”

22 NIH ICs currently offer K99/R00 grants– but with different requirements, funding levels and “enthusiasm”

○NHLBI: K99 PIs were more successful in obtaining subsequent grant support than the other groups, including other K awardees.

○NIGMS: The jury is still out on whether K99/R00’s are achieving their goals or if we have just created a new caste system and would be better off using the money to fund ESI R01s.

“The K99 is not intended to extend time in the postdoctoral lab while an individual is on the job market. individuals who are testing the academic job market are not the intended candidates for the grant mechanism.”

K99/R00 – one mechanism, many flavors

2017:	IC	# Reviewed	# Awarded	Success rate	2017 funds
	NCI	160	29	18.1%	\$3,948,618
	NHLBI	99	24	24.2%	\$3,072,290
	NIDCR	20	8	40.0%	\$1,088,762
	NIDDK	40	9	22.5%	\$815,663
	NINDS	78	7	9.0%	\$626,346
	NIAID	55	4	7.3%	\$492,090
	NIGMS	103	20	19.4%	\$1,795,542
	NICHD	66	23	34.8%	\$2,614,951
	NEI	19	9	47.4%	\$888,860
	NIEHS	30	11	36.7%	\$1,170,586
	NIA	67	28	41.8%	\$3,207,904
	NIAMS	22	5	22.7%	\$460,636
	NIDCD	16	3	18.8%	\$347,921
	NIMH	78	16	20.5%	\$1,871,170
	NIDA	52	10	19.2%	\$1,444,042
	NIAAA	26	11	42.3%	\$1,491,773
	NINR	10	2	20.0%	\$181,258
	NHGRI	19	7	36.8%	\$910,667
	NIBIB	30	5	16.7%	\$409,857
	NCCIH****	5	3	60.0%	\$327,599
	NIMHD***	4	1	25.0%	\$90,386
	NLM	5	0	0.0%	\$0
	OD ORIP-SEPA†	1	0	0.0%	\$0
	Activity Total	1,005	235	23.4%	\$27,256,921

What if we provide “Need-to-Know”?? Potential outcomes

PhD students:

- Specialized expertise embedded in broad literacy
- “Research toolbox”
- Mentored original research, team based
- Communicate impact to peers and public
- Working familiarity with career options

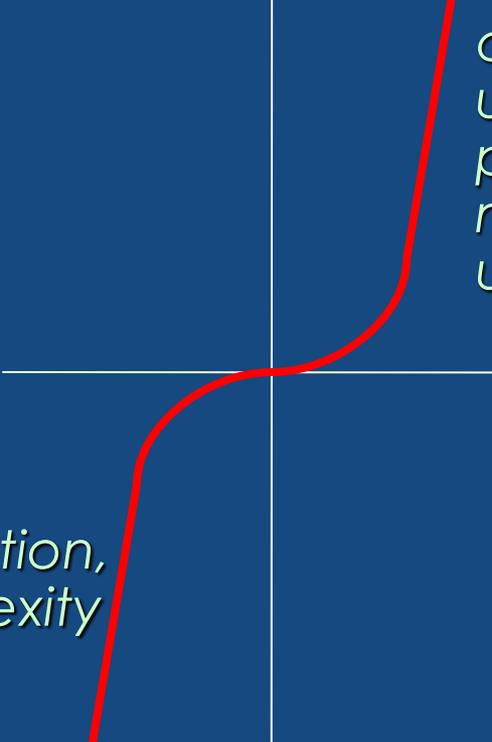
Postdocs:

- Skills for the practice of science
- Skills for independent research and support for the transition

Potential outcomes:

- Informed, empowered trainees
- Postdoc education mission
- Teams do bold, exciting research
- Appropriate training for nextgen bioscience leaders
- Postdoc population more market appropriate
- Other career options driven by evolving markets
- Greatly reduced training period: *4-8 years total*
- Lab demographics change
- University of the Future

21st century bioscience at an inflection point



*data collection,
detailed description,
resolving complexity*

*achieve mechanistic
understanding enabling
prediction and
manipulation; address
urgent societal issues*

We need biosciences trainees empowered:

- *to make bold, fundamental discoveries*
- *to communicate the excitement and importance of the discoveries*
- *to enable application of discoveries to societal challenges*

Transition to the Independent Phase of the Pathway to Independence Award (R00)

The transition is NOT guaranteed.

It is subject to review of:

- Success of the awardees' research progress and accomplishments
- K99 phase mentor's statement
- Evaluation of the research plan to be carried out at the extramural sponsoring institution at which he or she has been recruited
- Institutional commitment to the candidate
- Plans for his/her career development

Activating the Independent Phase of the Pathway to Independence Award (R00)

- **Area of research**

- Relevant to the mission of the NIH awarding component that funded the K99 phase.

- **Institution**

- Apply for positions at institutions different from where the mentored research was conducted (encouraged, not required). Provide a plan by which you will advance to independence.

Acceptability of a specific independent position for the R00 phase of the award

- **An institutional commitment agreement** stating that the appointment
 - is a tenure-track or equivalent
 - is not contingent on the transfer of the award to the institution.
- The sponsoring institution should **not** require the use of R00 funds to offset a typical startup package.
- The institution must foster and support the awardee's ability to apply for and secure independent research grant (R01) support.
- Contact NIH staff to review your start-up package **prior** to activating the independent phase of the award. NIH will not activate the independent phase if the institutional commitment is deemed inadequate.
- **Keep in mind:** \$249,000 = **total** costs.

Anticipated time frame to transition to R00 phase

- Complete at least one full year of mentored training under the K99 phase before transitioning to the R00 phase, “*except under unusual circumstances*”. (Otherwise consider alternatives: K22, R03, R21, or R01).
- May request a **No Cost Extension** but not supplements to extend K99 phase.
- Continuity in time
- Submit the R00 application no later than 2 months prior to the proposed activation date of the R00 award by the R00 phase grantee organization.
- Contact NIH program officials to discuss plans for transition **not later than 6 months** prior to the termination of the K99 phase

The R00 application must include:

- A new face page signed by the R00 phase institutional representative;
- A new project description page (the project summary or abstract should be updated to reflect current plans for the R00 phase);
- Detailed budget pages for a non-modular budget;
- Biographical sketches for the PD/PI and any other Key Personnel;
- A new Resources page;
- A brief description of progress made during the K99 phase that will serve as the Final Progress Report for the K99 phase;

The R00 application must include:

- An updated research plan (the specific aims should be updated to reflect current plans for the R00 phase, and the updated research plan should be described in **less than 5 pages**);
- Updated Protections for Human Subjects and Inclusion of Women, Minorities and Children (as appropriate);
- Updated Vertebrate Animals (as appropriate);
- Updated Biohazards (as appropriate); and
- A new checklist.