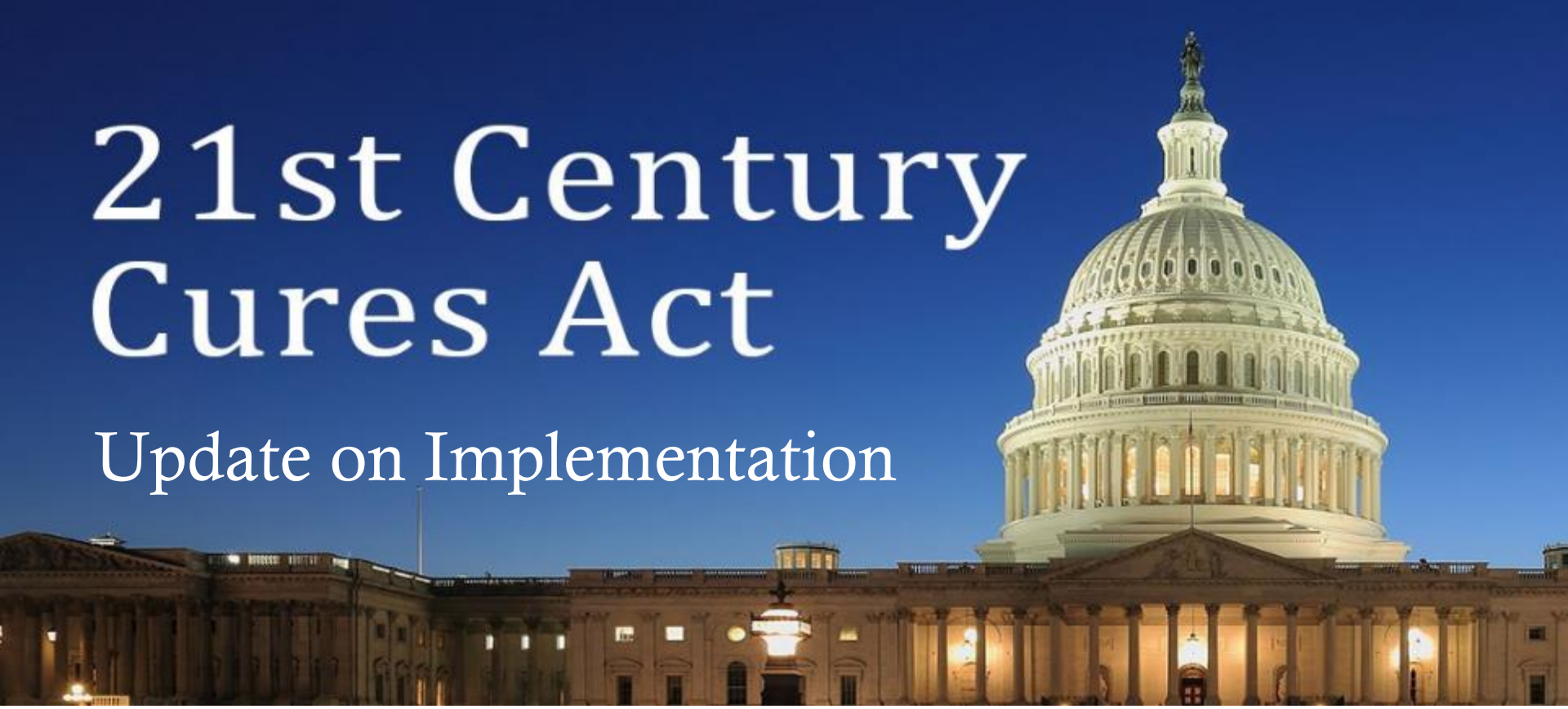


21st Century Cures Act

Update on Implementation

Patricia Brown, OLAW, NIH

Betty Goldentyer, USDA, APHIS, Animal Care

Brianna Skinner, FDA

March 2021

21st Century Cures Act
NIH Actions

Patricia Brown, VMD, MS, DACLAM
Director Office of Laboratory Animal Welfare, NIH

21st Century Cures Act in a Nutshell

Comprehensive legislation passed in 2016

Intent: advance biomedical research from basic research to advanced clinical trials

Intent: streamline drug approval

21st Century Cures Act in a Nutshell

Mandates federal efforts to reduce administrative burden for researchers

Section 2034(d) assigns NIH as lead agency in cooperation with USDA and FDA to focus on animal care and use in research

What Does 2034(d) Ask?

The Director of the NIH, in collaboration with the Secretary of Agriculture and the FDA Commissioner, shall complete a review of applicable regulations and policies for the care and use of laboratory animals and make revisions, as appropriate, to:

reduce administrative burden on investigators

while maintaining the **integrity and credibility of research** findings

and **protection of research animals**

Working Group Timeline

2017

Working Group convened; reviewed relevant policies and regulations

2018

Held listening sessions

Released Request for Information (RFI) for public comment in March

Released draft report in December

2019

Final report published in August

Find the final report and more at:

https://olaw.nih.gov/21st-century-cures-act.htm

NIH Steps: Update Guidance

- RFI on Use of AAALAC Program Description in OLAW Assurance

  NOT-OD-20-169

- RFI on Clarification of Institutional Responsibilities Regarding Grant to Protocol Congruency

  NOT-OD-20-153

- RFI on Flexibilities for Conducting Semiannual Animal Facility Inspections

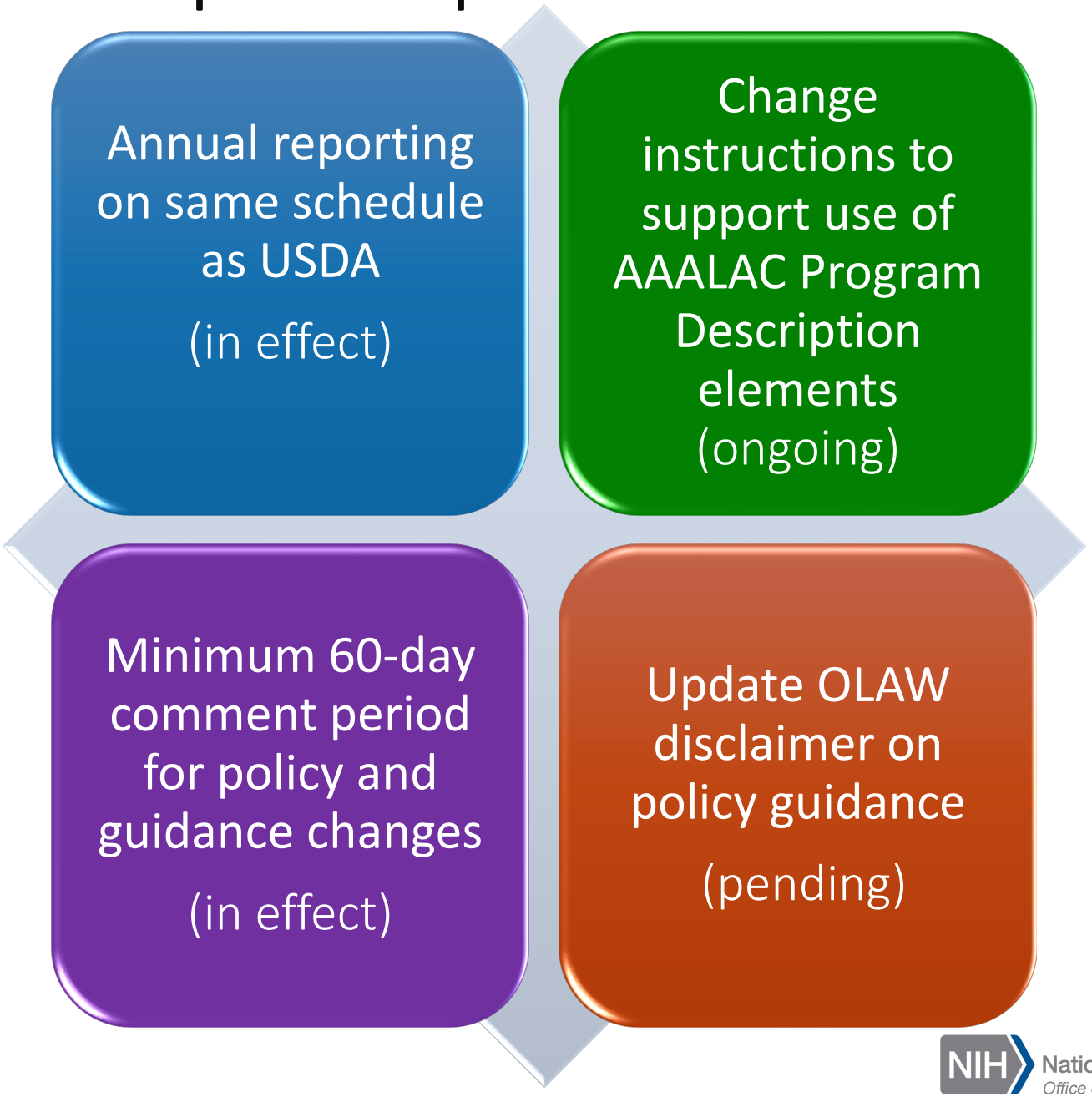
  NOT-OD-20-145

Photo: https://fbresearch.org/wp-content/uploads/2018/03/FullSize_Poster_Mice.jpg

NIH Steps: Update Guidance

- Use of DMR for low-risk activities and VVC for significant changes
- What is exempt from IACUC review
- Options for IACUC review of non-pharmaceutical grade substances
- Reporting noncompliance
- Departures from the *Guide*
- Applicability of the PHS Policy to zebrafish immediately after hatching

NIH Steps to Improve Coordination



More NIH Steps to Improve Coordination

Engage

- ✓Engage with DoD and VA to harmonize

Support

- ✓Support industry-led training and resources:
  - ➢Training IACUCs to reduce burden (ICARE, IACUC 101, SCAW, PRIM&R)
  - ➢CUSP through FDP
  - ➢Universal Protocol Template (UPT) through FDP
  - ➢IACUC best practices through IAA

Update

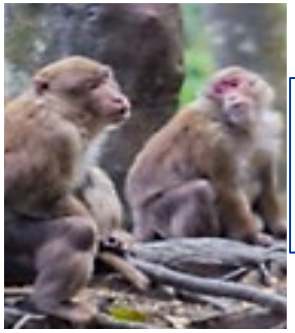
- ✓Update OLAW website resources

21st Century Cures Act
USDA APHIS Actions

Betty Goldentyer, DVM
USDA, APHIS, Animal Care

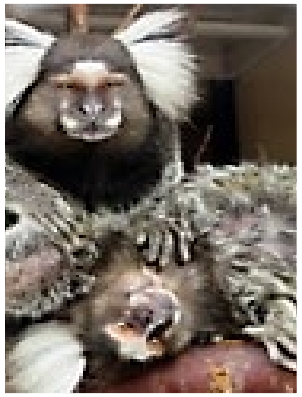
USDA United States Department of Agriculture

USDA Steps to Reduce Burden



Proposed Rule for Comment:
9/17/2020 to 11/16/2020

Animal Welfare Act: Research Facility Registration Updates, Continuous Reviews, and Annual Reports



61 Comments received

USDA Steps to Reduce Burden: Proposed Rule

Section 2.31(d)(5): Remove the requirement for the IACUC to conduct continuing reviews of activities not less than annually and replace it with a complete review of approved activities every 3 years

USDA Steps to Reduce Burden: Proposed Rule

Section 2.36(a): Eliminate the requirement for Chief Executive Officer (CEO) and Institutional Official (IO) signatures on the annual report submitted in paper form

USDA Steps to Reduce Burden, Proposed Rule (continued)

Section 2.30:

- Eliminates the 3-year registration renewal
- Adds a provision that clarifies the duration of a research facility's registration and conditions for its cancellation.
- Removes inactive status

Awaiting Departmental clearance to publish a Final Rule

Steps to Reduce Burden

https://en.wikipedia.org/wiki/File:Dog_stretch_wb.jpg/

Flexibilities:

Current flexibilities available to IACUCs regarding semiannual inspections include:

- Use of consultant
- Efficient use of IACUC members
- ~~Virtual inspections using live video feed~~
- Use of a AAALAC site visit

Steps to Reduce Burden: Reporting

USDA developed an online portal for submitting annual reports with user input to streamline data submission.

NIH and USDA will work together to have annual reporting to both agencies on the same reporting schedule through a shared portal.

https://www.picpedia.org/post-it-note/a/annual-report.html

USDA Steps to Reduce Burden: Guidance

Significant new guidance and revisions will be made available for public comment.

New guidance will include a statement that they are meant to be clarifications of the AWA and Animal Welfare Regulations, and therefore,

NOT legally binding.

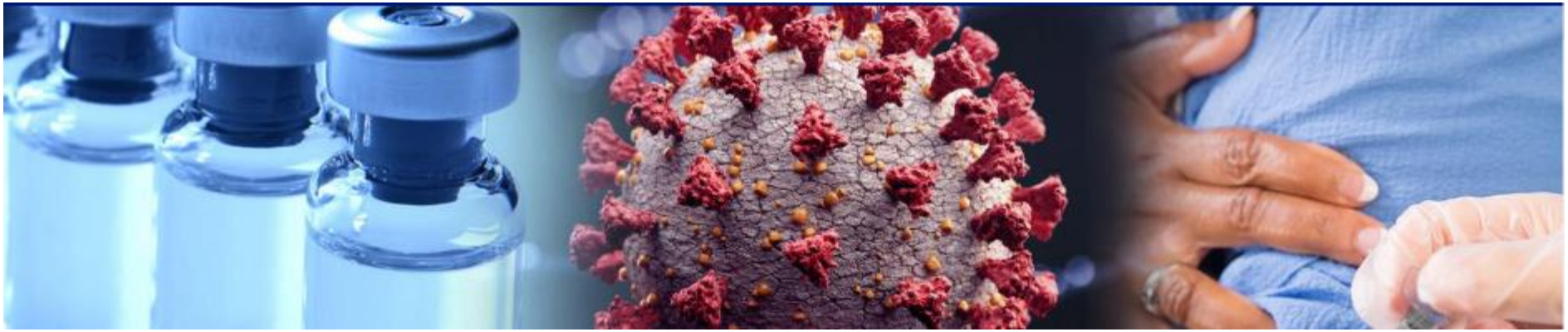
https://picpedia.org/handwriting/f/feedback.html

21st Century Cures Act
FDA Actions

Brianna Skinner, DVM, MPH
FDA, OCET, Office of the Commissioner

FDA Steps to Reduce Burden

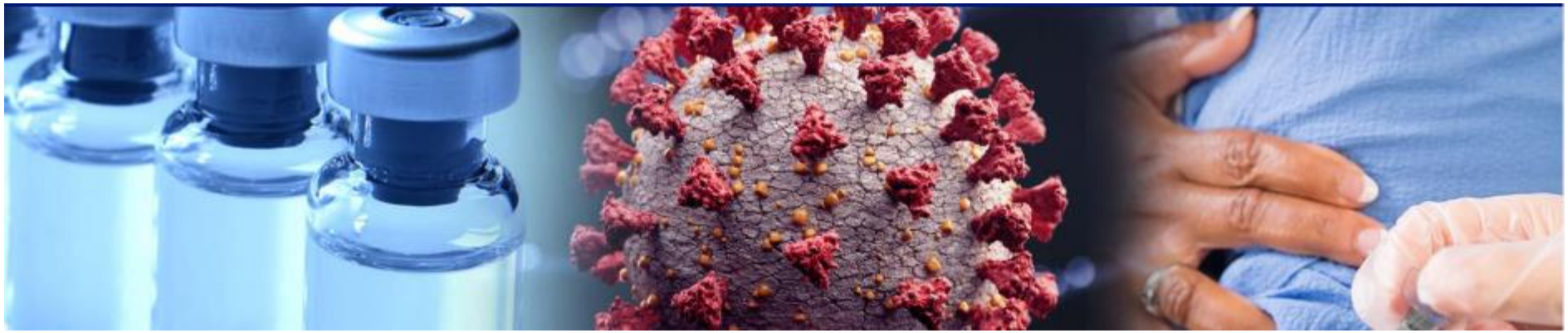
FDA's rulemaking with respect to part 58, GLP for Nonclinical Laboratory Studies is still ongoing...



Comments made in response to the 21st Century Cures Act RFI regarding the subject of the GLP rulemaking is being reviewed as finalization of the proposed rule is considered

FDA Steps to Reduce Burden, continued

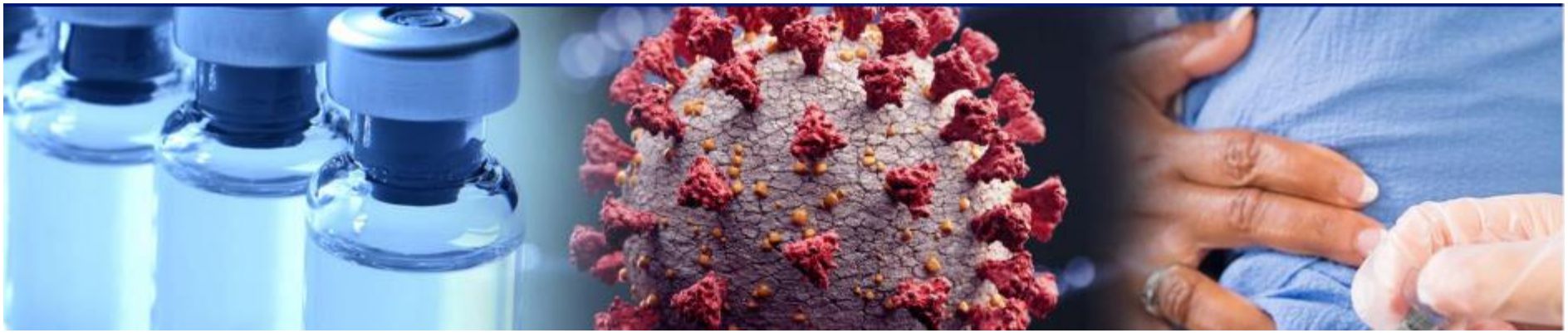
NIH OLAW will review and update the guidance on non-pharmaceutical grade substances to further clarify the options for IACUC review.



NIH OLAW will enlist the expertise of the FDA in the effort and seek public comment on the updated guidance.

FDA Steps to Reduce Burden, continued

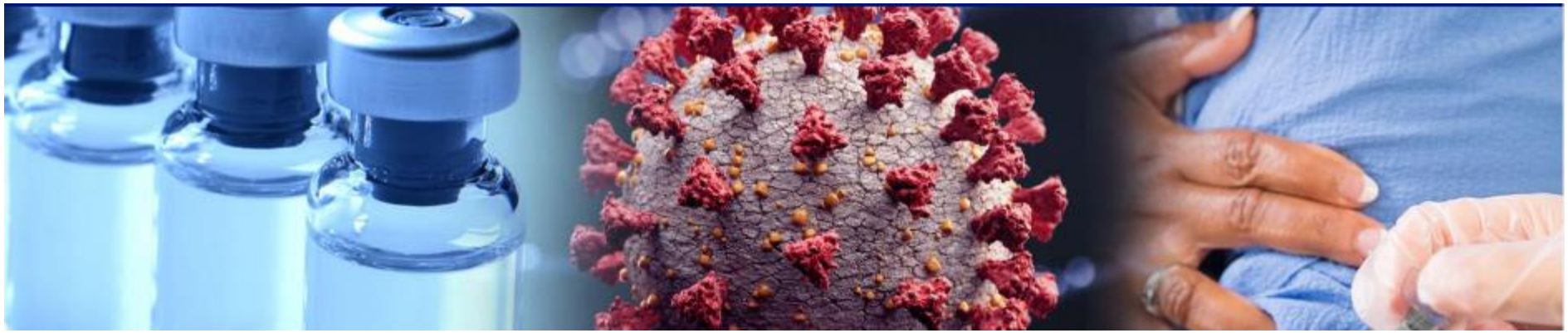
FDA has statutory authority to regulate drugs, including compounded drugs from bulk substances.



The Food and Drug Administration Modernization Act of 1997 (FDAMA) and the Drug Quality and Security Act (DQSA) amended the Federal Food, Drug, and Cosmetic (FD&C) Act with provisions addressing compounding drugs.

FDA Steps to Reduce Burden, continued

Compounded animal drug – made by combining, mixing, or altering ingredients to create a medication.



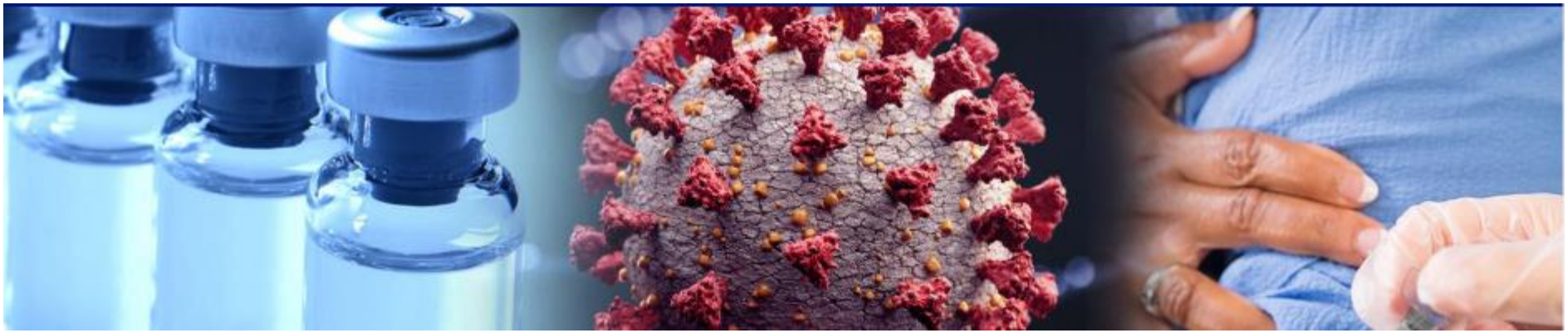
Compounded animal drugs are not FDA-approved

Approval means data were reviewed for a finished drug product manufactured and labeled in a particular way

Becomes part of a post-approval pharmacovigilance program.

FDA Steps to Reduce Burden, continued

Source of animal drug compounds – approved drug substance vs bulk drug substance.

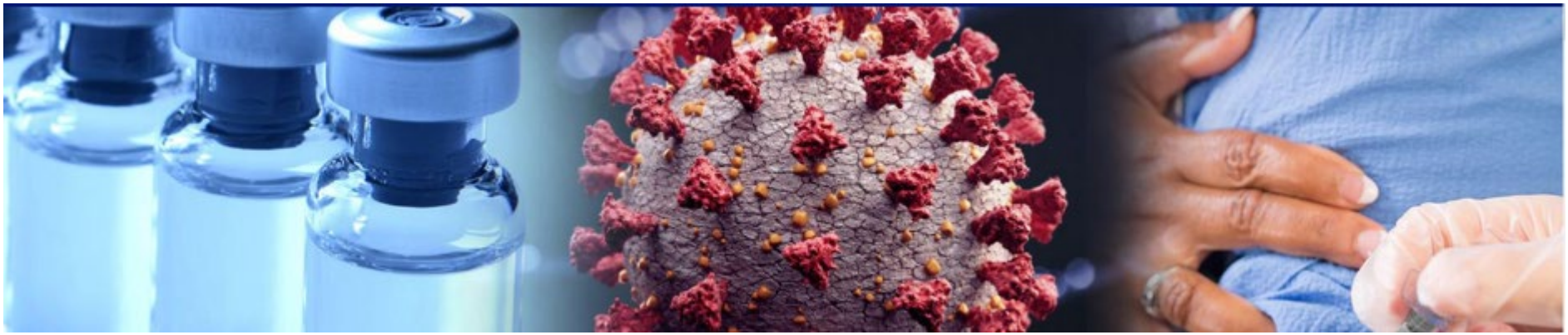


Compounding permitted when source of active ingredient is finished, FDA-approved drug.

Animal drugs compounded from bulk substances are not lawful under the FD&C Act.

FDA Steps to Reduce Burden, continued

November 19, 2019, the Center for Veterinary Medicine (CVM) issued draft Guidance for Industry #256, titled "Compounding Animal Drugs from Bulk Drug Substances."



Describes animal drug compounding enforcement priorities under which FDA **does not intend to take action** for certain violations of the FD&C Act.

FDA Steps to Reduce Burden, continued

FDA is most concerned with drugs compounded from bulk drug substances that:

present human or animal safety concerns

are for use in food producing animals

FDA Steps to Reduce Burden, continued

FDA is most concerned with drugs compounded from bulk drug substances that:

are copies of approved, conditionally approved, or indexed marketed animal drugs

are compounded without a patient-specific prescription

If the guidance is finalized, FDA intends to prioritize enforcement actions against these products.

FDA Steps to Reduce Burden, continued

Veterinarians would be able to write patient-specific prescriptions for animal drugs compounded from bulk drug substances for non-food-producing animals as long as, among other things:

the patient or group of patients is identified on the prescription;

and

the compounded drug is not a copy of an FDA-approved product.

FDA Steps to Reduce Burden, continued

The draft guidance would establish a list of bulk drug substances that can be used to compound:

office stock veterinarians need to have on hand for emergencies to treat non-food-producing animals,

and

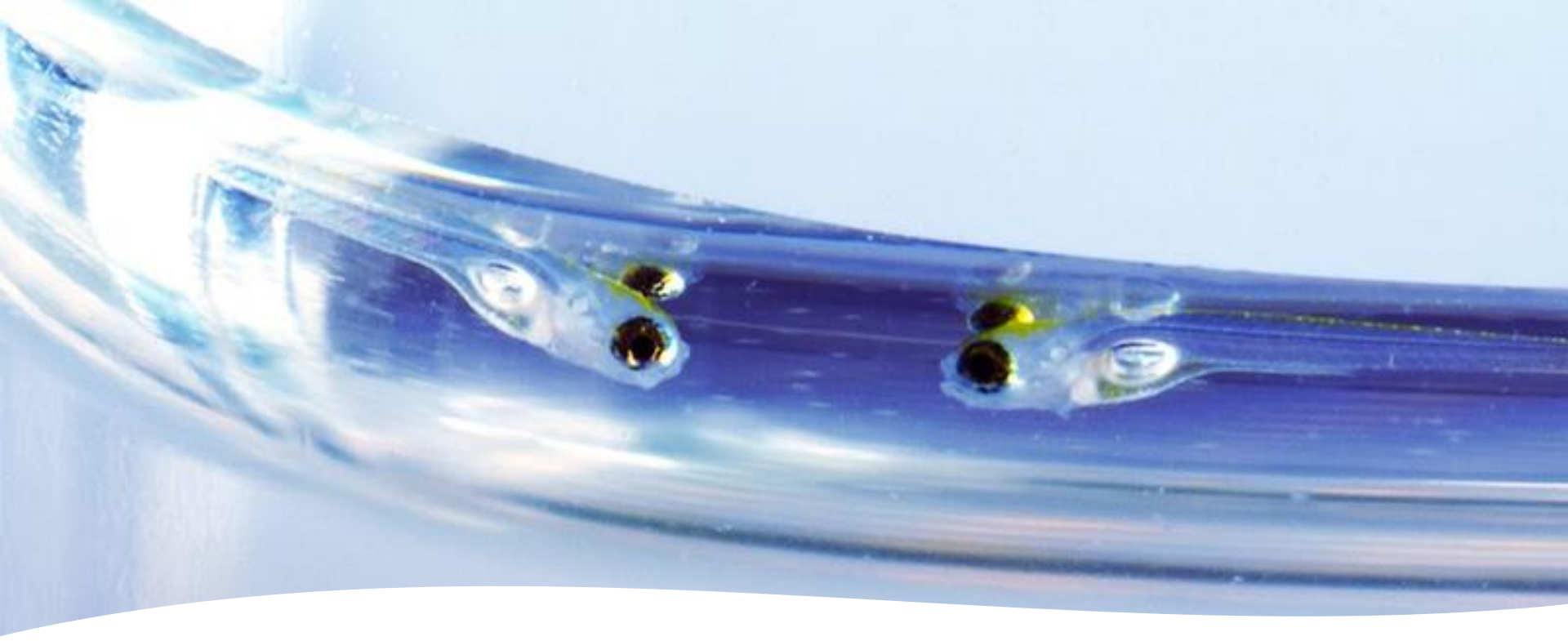
antidotes for food-producing animals.

This list does not apply to compounding from bulk drug substances for patient-specific prescriptions.

FDA Steps to Reduce Burden, continued

Over 1,400 comments were received; public comment period extended to October 15, 2020.

CVM is currently reviewing comments including submissions from AALAS and NIH OLAW.



21st Century Cures Act Implementation Summary

Efforts are ongoing

Public engagement throughout the process

Plans to evaluate the outcome of the efforts

OLAW Q&A:

Question 1:

How will you engage with stakeholders while implementing 21 CCA action items?

OLAW Q&A:

Answer to Question 1:

As we have with the development of the report the three agencies will continue to offer the public a comment period as new policies and new guidance are announced. The comments are very important in helping us shape the final versions of the policies and guidance that is developed.

USDA Q&A

Question 2:

When can we stop conducting the annual continuing reviews?

USDA Q&A

Answer to Question 2:

Not yet. This requires a regulatory change and that takes time. The process includes a proposed rule for public comment, a review of the comments and any necessary adjustments, then a final rule can be published with an effective date. We will keep you informed every step of the way. Until there is a new final rule, the current regulation is in effect.

USDA Q&A

Question 3:

What is the status of the USDA AC Policy Manual revision and opportunity for public comment?

Since the delays have been so extensive, leaving animals vulnerable, would USDA consider a more prudent and practical process? Namely, might it conduct a review of each policy while the other policies remain in place?

USDA Q&A

Answer to Question 3:

We are going to be moving very deliberately and transparently as we review and re-propose the policies. I think you'll see one policy at a time posted for review and comment. Once we have completed the opportunity for comment, and we make sure there is no added burden or regulatory overreach, we'll post them as they are approved. Some of the previous policies are no longer needed and probably won't come back but we do recognize that some of the topics were helpful in clarifying the regulations and we're working through those.

Working Group Q&A

Question 4:

How do you intend to evaluate the Working Group's ongoing efforts to reduce administrative burden?

Working Group Q&A

Answer to Question 4:

We will be enlisting an evaluation team to gather input from researchers, IACUC members and animal care and use program representatives. Our plan is to engage with key representatives from scientific and professional organizations and use their leverage with their constituents to develop and distribute the surveys and gather information on the effectiveness of the agencies actions in reducing the administrative burden on researchers.

Working Group Q&A

Question 5:

How will the process to reduce regulatory burden ensure that animal welfare best practices will never be at the expense of reducing administrative burden or political expediency?

Working Group Q&A

Answer to Question 5:

The Working Group, from the very beginning of this effort has made animal welfare the top priority and will continue to do so.

FDA Q&A

Question 6:

At what stage are the GLP rules under review?

When will the next version of the GLP rules be available for review by the public?

FDA Q&A

Answer to Question 6:

FDA is still reviewing comments to the proposed rulemaking. FDA will coordinate with NIH and USDA as per MOU for the final clearance before the final rule is published.

FDA Q&A

Question 7:

What Act gives FDA the statutory authority to regulate new animal drugs?

FDA Q&A

Answer to Question 7:

The Federal Food, Drug and Cosmetic Act (FD&C Act) gives FDA the authority to regulate new animal drugs, which includes animal drugs compounded from bulk drug substances.

FDA Q&A

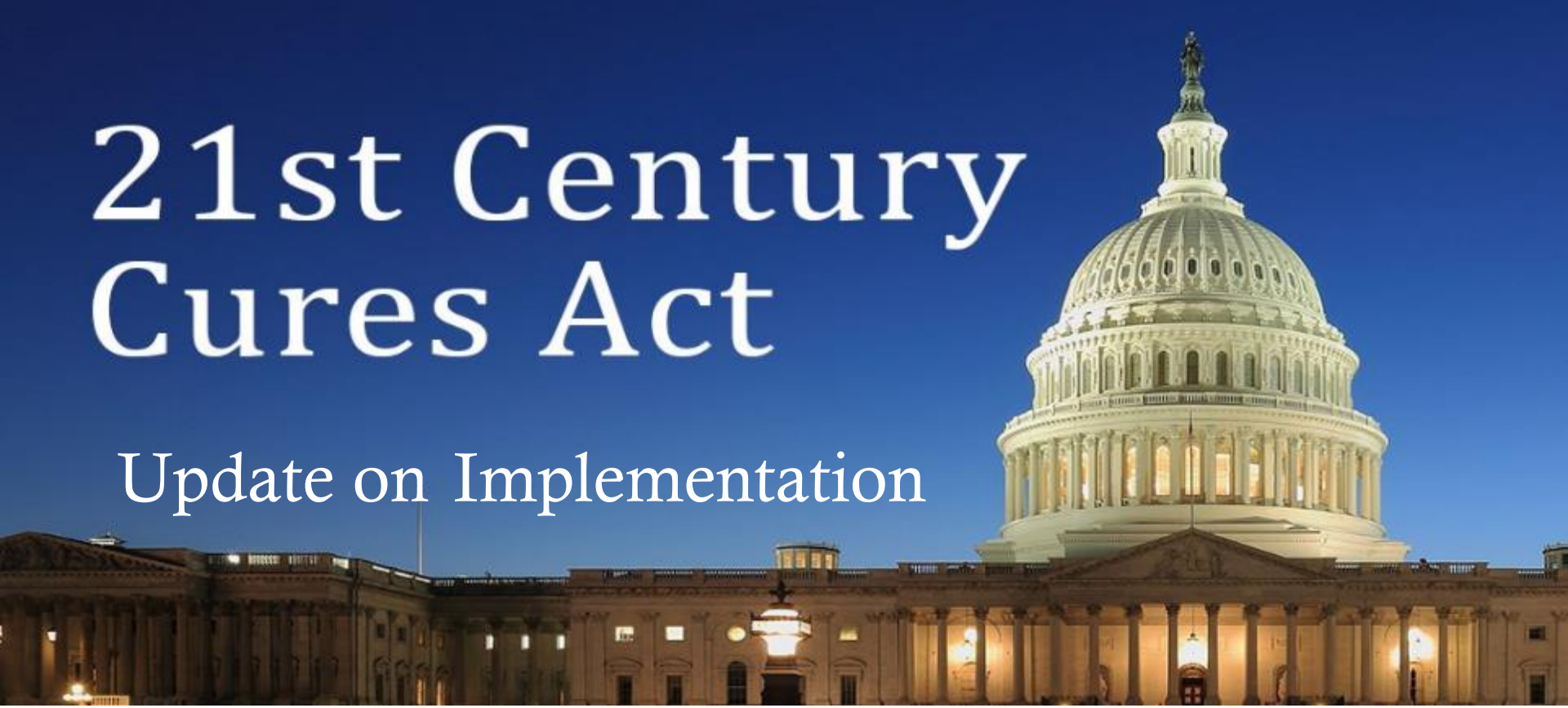
Question 8:

What draft guidance, if finalized, would describe FDA's animal drug compounding enforcement priorities?

FDA Q&A

Answer to Question 8:

The draft Guidance for Industry #256, titled "Compounding Animal Drugs from Bulk Drug Substances," if finalized, would describe FDA's animal drug compounding enforcement priorities and advise veterinarians, pharmacists, and the public on circumstances under which FDA does not intend to take action for certain violations of the FD&C Act, when pharmacists and veterinarians compound or oversee the compounding of animal drugs from a bulk drug substance.



Patricia Brown, OLAW, NIH

Betty Goldentyer, USDA, APHIS, Animal Care

Brianna Skinner, FDA

Next OLAW Webinar

June 2021

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