From: Gibbens, Robert - MRP-APHIS
To: Morse, Brent (NIH/OD) [E]
Subject: RE: PCRM allegations at UAMS
Date: Saturday, January 7, 2023 8:35:00 AM
Attachments: image001.png

Hi Brent - - we are still gathering some additional information. I've copied the area supervisor's (Dr. David Sabala) email explaining the status below. "Courtney" referred to in the email is Dr. Courtney Jernigan, the VMO assigned to the facility(s). As we get further information or clarification, I'll let you know.....Bob

Robert M. Gibbens, DVM
Director, Animal Welfare Operations
USDA, APHIS, Animal Care
2150 Centre Avenue, Bldg. B
Ft. Collins, CO 80526
(b) (6)

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-----Original Message-----
From: Sabala, David - MRP-APHIS david.l.sabala@usda.gov
Sent: Thursday, January 5, 2023 5:53 PM
To: Gibbens, Robert - MRP-APHIS robert.m.gibbens@usda.gov
Subject: RE: [External Email]Use of Animals for Human Infant Microbiome Research at the University of Arkansas,for Medical Sciences

What Courtney was told by the AV was that these protocols were not conducted by UAMS or at UAMS, they were Children's Research protocols. The AV is also the AV of Arkansas Children's Research institute. My understanding from Courtney is that there may be members of both IACUC's that are the same. I will need to find out what the composition of both are. Both facilities are in Little Rock so there could be some crossover. But her understanding when she called the AV was that the protocols were conducted under Arkansas Children's Research Institute and approved by the Children's Research IACUC.

When she conducted the inspection of UAMS in August, there was no regulated activity because the facility was being renovated. They did not have any animals for the past two years and no pigs in recent memory. Based on her focused inspection of records and protocol review in August, she did not remember anything related to this complaint. So when we received the complaint, we discussed it and determined that we would wait a while, hoping they would complete renovations soon , re-inspect and then discuss the complaint with them. So no, since Courtney did not see any issues related to the complaint at her inspection, we would wait to check on it as I explained above. Arkansas Children's Research Institute was not even involved or considered until she talked to the AV this morning.

Now that she has contacted the AV and found out that the protocols were conducted at Children's Research, she will need to contact this facility as well. If the AV is right in stating that this activity

occurred a few years back, hopefully those records are available.
Courtney will now visit both facilities and see if there is any agreements or cooperative activity between the two, or if this was only Children's Research. I guess this could have been a cooperative study between the two facilities?

David

From: Gibbens, Robert - MRP-APHIS
Sent: Wednesday, December 21, 2022 10:44 AM
To: Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>
Subject: RE: PCRM allegations at UAMS

Hi Brent. Both the VMO and the supervisor are on leave until January; so I won't be able to provide details until then. Hope you have Merry Christmas and Happy New Year (or whatever you celebrate for the holidays).

Bob

Robert M. Gibbens, DVM
Director, Animal Welfare Operations
USDA, APHIS, Animal Care
2150 Centre Avenue, Bldg. B
Ft. Collins, CO 80526
(b) (6)


Join the Animal Care Stakeholder Registry and receive emails on topics of interest

---

From: Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>
Sent: Wednesday, December 21, 2022 8:09 AM
To: Gibbens, Robert - MRP-APHIS <robert.m.gibbens@usda.gov>
Subject: RE: PCRM allegations at UAMS

Hello Bob,

Just checking to see if you have any conclusions regarding this issue. No hurry. Just following-up.

Best regards, Brent

Brent C. Morse, DVM, DACLAM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare

National Institutes of Health

From: Gibbens, Robert - MRP-APHIS <robert.m.gibbens@usda.gov>
Sent: Wednesday, October 26, 2022 5:54 PM
To: Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>
Subject: [EXTERNAL] RE: PCRM allegations at UAMS

Hi Brent. We haven't requested a formal investigation, but we are sending a VMO to the facility to look into it. I'll do my best to let you know when we've done that, but if you haven't heard from me in a couple of weeks, please feel free to circle back with me. Thanks.....Bob

Robert M. Gibbens, DVM
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USDA, APHIS, Animal Care
2150 Centre Avenue, Bldg. B
Ft. Collins, CO 80526
(b) (6)


Join the Animal Care Stakeholder Registry and receive emails on topics of interest

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From: Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>
Sent: Wednesday, October 26, 2022 1:15 PM
To: Gibbens, Robert - MRP-APHIS <robert.m.gibbens@usda.gov>
Subject: PCRM allegations at UAMS

Hi Bob,

Regarding the attached letters to you and Pat Brown, are you investigating the allegations further? In the spring of this year, I copied you on our final letter to UAMS regarding a January 2022 PCRM letter to NIH covering essentially the same allegations. I don't think the attached letters contain any further substantive allegations. If you are investigating, I'll keep the OLAW case open until your investigation is completed. If not, I will close the case with no further action. Let me know when you can. Thanks.

Sincerely, Brent

Brent C. Morse, DVM, DACLAM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

From: Gibbens, Robert - MRP-APHIS
To: Morse, Brent (NIH/OD) [E]
Subject: RE: PCRM allegations at UAMS
Date: Wednesday, December 21, 2022 10:44:00 AM
Attachments: image001.png

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Bob

Robert M. Gibbens, DVM
Director, Animal Welfare Operations
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Sincerely, Brent

Brent C. Morse, DVM, DACLAM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

From: Morse, Brent (NIH/OD) [E]
To: Gibbens, Robert - MRP-APHIS
Subject: RE: PCRM allegations at UAMS
Date: Wednesday, December 21, 2022 10:10:31 AM
Attachments: image001.png

Hello Bob,

Just checking to see if you have any conclusions regarding this issue. No hurry. Just following-up.

Best regards, Brent

Brent C. Morse, DVM, DACLAM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

From: Gibbens, Robert - MRP-APHIS <robert.m.gibbens@usda.gov>
Sent: Wednesday, October 26, 2022 5:54 PM
To: Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>
Subject: [EXTERNAL] RE: PCRM allegations at UAMS

Hi Brent. We haven't requested a formal investigation, but we are sending a VMO to the facility to look into it. I'll do my best to let you know when we've done that, but if you haven't heard from me in a couple of weeks, please feel free to circle back with me. Thanks.....Bob

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Sincerely, Brent

Brent C. Morse, DVM, DACLAM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

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Subject: RE: PCRM allegations at UAMS
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Attachments: image001.png

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Sincerely, Brent

Brent C. Morse, DVM, DACLAM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

From: Morse, Brent (NIH/OD) [E]
To: Gibbens, Robert - MRP-APHIS
Subject: PCRM allegations at UAMS
Date: Wednesday, October 26, 2022 3:15:13 PM
Attachments: 2860_001.pdf

Hi Bob,

Regarding the attached letters to you and Pat Brown, are you investigating the allegations further? In the spring of this year, I copied you on our final letter to UAMS regarding a January 2022 PCRM letter to NIH covering essentially the same allegations. I don't think the attached letters contain any further substantive allegations. If you are investigating, I'll keep the OLAW case open until your investigation is completed. If not, I will close the case with no further action. Let me know when you can. Thanks.

Sincerely, Brent

Brent C. Morse, DVM, DACLAM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

A3063-1M

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October13, 2022

Robert Gibbens, DVM
Director, Animal Welfare Operations
USDA/APHIS/Animal Care
2150 Centre Ave.
Building B, Mailstop 3W11
Fort Collins, CO 80526-8117

Patricia A. Brown, V.M.D., M.S.
Director, Office of Laboratory Animal Welfare
National Institutes of Health
RKL 1, Suite 360, MSC 7982
6705 Rockledge Dr.
Bethesda, MD 20892-7982

Submitted by email (brownp@od.nih.gov; robert.m.gibbens@aphis.usda.gov)

Re: Use of Animals for Human Infant Microbiome Research at the University of Arkansas for Medical Sciences

Dear Dr. Gibbens and Dr. Brown:

The Physicians Committee for Responsible Medicine requests that the United States Department of Agriculture's (USDA) Animal and Plant Health Inspection Service (APHIS) and the National Institutes of Health's Office of Laboratory Animal Welfare (OLAW) investigate the killing of 22 piglets by the University of Arkansas for Medical Sciences (UAMS) to study neonatal diets, where all endpoints could have been studied using humans and human-relevant approaches. In this case, experimenters at UAMS fed 22 neonatal piglets either pasteurized human milk or dairy-based infant formula. At twenty-one days old, experimenters killed the piglets and removed their intestinal contents to analyze the effect on gut microbiomes.[1]

The University of Arkansas for Medical Sciences' animal use is at odds with the current standards of practice in infant formula research in the United States where endpoints are routinely studied in humans. The comparison of gut microbiota in breastfed and formula-fed human infants has been studied extensively. However, this study retreats from the species of interest (humans) to examine pigs—a step backward in terms of scientific relevance. The use of animals here demonstrates both a lack of scientific merit and research misconduct under the Animal Welfare Act.

Under the Animal Welfare Act, UAMS meets the statutory definition of a "research facility" and is therefore required to comply with the statute's regulations and standards. As part of this required compliance, any use of live animals for research, testing, or training must be approved by UAMS' Institutional Animal Care and Use Committee (IACUC). The university is currently registered with the USDA under certificate number 71-R-0011. The Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy) requires that institutions have an OLAW-approved Animal Welfare Assurance before carrying out any activities involving live vertebrate animals. The UAMS OLAW assurance is D16-00035 (A3063-01).

The Physicians Committee believes that inadequate oversight by UAMS' IACUC is responsible for the improper approval and ongoing use of live animals for infant formula research. The specific regulatory violations follow.

1. Use of Animals to Study Human Nutrition Not "Scientifically Valuable Research"

Section 2143 of the Animal Welfare Act and C.F.R. Title 9, Section 2.31(e) of the Animal Welfare Act's implementing regulations state that a proposal to conduct an activity involving animals must describe "procedures designed to assure that discomfort and pain to animals will be limited to that which is unavoidable for the conduct of scientifically valuable research." **Studying pigs to understand how infant formulas affect gut bacteria is not scientifically valuable research when such research can and has been safely performed directly on humans. Dairy-based infant formulas have been extensively studied in human infants, including their effects on gut microbes relative to breastfeeding. UAMS's animal use here is convoluted and at odds with the current standards of practice in human nutrition research.**

This research also has several design flaws that diminish the significance and reproducibility of the results. It is broadly accepted that breast milk is a major influence in the development of healthy gut microbiota. However, this study fails to mimic the importance of the mode (breastfeeding vs. bottle-feeding) and duration of feeding. Additionally, this study used human milk samples collected from two to twelve months of lactation, and different components were added to the piglet's diet to maintain the nutrient requirements. These variations in the milk composition and diet might affect the microbiota composition and protein expression of the gut microbiota.

Experimenters describe the study as "preclinical," reflecting their intention to apply the results to human clinical populations. Clearly, using animals here represents a significant step backward in terms of the scientific value of this study relative to human and *in vitro* models. As detailed below, infant formulas have been extensively studied in human clinical trials.

2. UAMS' Justification of Animal Use Is Insufficient Because Alternatives Exist

Section 2143 of the Animal Welfare Act and C.F.R. Title 9, Section 2.31(d)(1)(i, ii) of the Animal Welfare Act's implementing regulations require that the principal investigator consider available alternatives to procedures that may cause more than momentary or slight pain or distress to any animal used for research or educational purposes.

The PI did not meet this requirement because there is no rationale for animal use in human nutrition research given the abundance of human studies examining the effects of infant formulas on human gut bacteria. Having not provided objective evidence to support the use of animal subjects where study of human subjects is common, ethical, and more relevant to the stated research goals, the PI did not meet this requirement of the Animal Welfare Act.

A proper alternatives search would have revealed nonanimal methods for infant formula research and an abundance of peer-reviewed literature demonstrating the equivalence or superiority of human biology-based models compared to animal use. Numerous studies have already reported on the impact of diet on gut bacteria and proteins using human infants and other human-relevance approaches. For example:

- A publication from the CHILD cohort study, including a subset of 1,249 mother-infant pairs, used a multi-analytic approach to associate breastfeeding practices and milk microbiota with infant gut microbiota, while controlling for relevant cofactors.[2]

- Another study used fecal bacterial composition to compare the gut microbiota of 91 infants who were exclusively breastfed or formula-fed and found significant differences in microbiota between the two groups.[3]

- Several meta-analyses, including one published in *Nature Communications*, have compared the gut microbiota of exclusively breastfed (EBF) and non-EBF infants across populations. This review examined seven microbiome studies with a total of 1,825 stool samples of 684 infants from five countries and found consistent differences between non-EBF and EBF infants in gut microbial diversity, microbiota age, microbial composition, and microbial predicted functional pathways. This meta-analysis clearly supports the fact that all endpoints can be studied in humans.[4]

- Several *in vitro* gut models have been developed and are being used to study human gut microbiota. Researchers have developed a gut model and are using it to study the interactions between bacteria and the cecal mucus commensal microbiota.[5]

- A novel 3D *in vitro* model of the human gut microbiota is being used to execute in-depth analyses concerning gut microbiota composition and production of metabolites and how these parameters alter in response to different factors.[6]

An abundance of alternatives to animal experiments were available to researchers here. This study could have been ethically conducted in human subjects or using *in vitro* models, more ethical methods and of far greater scientific and clinical relevance.

3. The Use of Animals for Infant Formula Research Is Not "Unavoidable"

The Animal Welfare Act also requires that activities involving animals be designed to "assure that discomfort and pain to animals will be limited to that which is unavoidable for the conduct of scientifically valuable research." 9 C.F.R. § 2.31(e)(4).

We believe that this requirement was not met by the PI because numerous clinical trials have already studied and reported the impact of breastmilk and infant formula on the microbiome. This clearly demonstrates that such use of live animals is not "unavoidable."

4. UAMS' IACUC Is Failing to Properly Oversee Animal Use

Section 2143 of the Animal Welfare Act and Title 9, Section 2.31(d)(1)(i, ii) of the Animal Welfare Act's implementing regulations require that the IACUC enforce the requirements described in items 1 through 3 above and thereby determine that the proposed activities are in accordance with the Animal Welfare Act and C.F.R Title 9, Section 2.31(d).

We believe that these requirements were not met by UAMS' IACUC because the animal use protocol was approved despite the violations described in items 1 through 4 above. Thus, the Physicians Committee alleges inadequate oversight by UAMS' IACUC.

5. PHS Policy and the *Guide*

Finally, the issues described above violate the PHS Policy and the *Guide for the Care and Use of Laboratory Animals* (the *Guide*). OLAW must evaluate allegations of noncompliance with the PHS Policy "and, as necessary, restrict or withdraw approval of [Animal Welfare] Assurances."

The PHS Policy's Principle II of the U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training emphasizes that "procedures involving animals should be designed and performed with due consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society." Principle III provides that "the animals selected for a procedure should be of an appropriate species and quality and the minimum number required to obtain valid results. Methods such as mathematical models, computer simulation, and in vitro biological systems should be considered."

As detailed above, this study fails to advance scientific knowledge or the good of society. Pigs were not an appropriate species here as this subject of inquiry has been extensively and safely studied in human infants.

Accordingly, the Physicians Committee requests that APHIS and OLAW investigate this matter and order corrective action and appropriate penalties.

Thank you for your attention.

Sincerely,

(b) (6)

Cc: (b) (6)
(b) (6) Jeff Wolchok, IACUC Chair, UAMS; Laxmi Yeruva, Research Leader, USDA Agricultural Research Service; Dr. Axel Wolff, Deputy Director, OLAW.

---

[1] Rosa F, Zybailov BL, Glazko GV, Rahmatallah Y, Byrum S, Mackintosh SG, Bowlin AK, Yeruva L. Milk Formula Diet Alters Bacterial and Host Protein Profile in Comparison to Human Milk Diet in Neonatal Piglet Model. *Nutrients*. 2021; 13(11):3718. https://doi.org/10.3390/nu13113718

[2] Fehr K, Moossavi S, Sbihi H, Boutin R, Bode L, Robertson B, et al. Breastmilk feeding practices are associated with the co-occurrence of bacteria in mothers' milk and the infant gut: The CHILD cohort study. *Cell Host & Microbe*. 2020;28(2):285-297.

[3] Ma J, Li Z, Zhang W, Zhang C, Zhang Y, Mei H, et al. Comparison of gut microbiota in exclusively breast-fed and formula-fed babies: A study of 91 term infants. *Sci Rep*. 20202;10(15792).

[4] Ho NT, Li F, Lee-Sarwar KA, Tun HM, Brown BP, Pannaraj PS, et al. Meta-analysis of effects of exclusive breastfeeding on infant gut microbiota across populations. *Nature Communications*. 2018;9(4169).

[5] Mokszycki ME, Leatham-Jensen M, Steggensen JL, Zhang Y, Krogfelt KA, Caldwell ME, et al. A simple in vitro gut model for studying the interaction between Escherichia coli and the intestinal commensal microbiota in cecal mucus. *Applied and Environmental Microbiology*. 2018;84(24).

[6] Biagin F, Calvigioni, M, Lapomarda A. Vecchione A, Magliaro C, Maria CD, et al. A novel 3D in vitro model of the human gut microbiota. *Sci Rep*. 2020;10(21499).

PhysiciansCommittee
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October 13, 2022

Robert Gibbens, DVM
Director, Animal Welfare Operations
USDA/APHIS/Animal Care
2150 Centre Ave.
Building B, Mailstop 3W11
Fort Collins, CO 80526-8117

Submitted by email (robert.m.gibbens@aphis.usda.gov)

Re: Use of Animals for Human Infant Nutrition Research at the University of Arkansas for Medical Sciences

Dear Dr. Gibbens:

The Physicians Committee for Responsible Medicine ("Physicians Committee") requests that the United States Department of Agriculture's (USDA) Animal and Plant Health Inspection Service (APHIS) investigate the killing of 30 piglets by the University of Arkansas for Medical Sciences (UAMS) to study the effects of several types of infant formula, all of which are commercially available and in wide clinical use, on human infants.

The University of Arkansas for Medical Sciences' animal use is at odds with the current standards of practice in infant formula research in the United States. This study sought to determine if soy formula stimulates estrogen production, leading to male reproductive toxicity. However, this study retreats from the species of interest (humans) to pigs, raising issues of both a lack of scientific merit and serious research misconduct. The goals of the study could have been accomplished without using animals. Numerous studies have already investigated the estrogenic effects of soy formula directly on human infants.

Under the Animal Welfare Act, UAMS meets the statutory definition of a "research facility" and is therefore required to comply with the statute's regulations and standards. As part of this required compliance, any use of live animals for research, testing, or training must be approved by UAMS' Institutional Animal Care and Use Committee (IACUC). The university is currently registered with the USDA under certification number 71-R-0011.

The Study

In this case, experimenters at UAMS used 30 male piglets to evaluate if soy formula stimulates estrogen and if it can alter male reproductive development. The study divided pigs into five groups fed either sow milk, Similac Advance powder (cow's milk-based formula), soy-based

formula, Similac Advanced supplemented with 2 mg/kg/d estradiol, or Similac Advance with pure genistein.[1]

After the three-week dietary intervention, all piglets were killed. Their blood was collected for isoflavones and hormone analysis, and their testis, prostate, and other tissues were weighed. The study concludes that soy formula is not estrogenic in the male neonatal piglet and that soy formula does not significantly alter male reproductive development. This study occurred despite extensive human studies into the estrogenic effects of both cow's milk-based infant formula and soy-based infant formula.

The Physicians Committee believes that inadequate oversight by UAMS' IACUC is responsible for the improper approval and ongoing use of live animals for infant formula research. The specific regulatory violations follow.

1. Use of Animals to Study Human Nutrition Not "Scientifically Valuable Research"

Section 2143 of the Animal Welfare Act and C.F.R. Title 9, Section 2.31(e) of the Animal Welfare Act's implementing regulations state that a proposal to conduct an activity involving animals must describe "procedures designed to assure that discomfort and pain to animals will be limited to that which is unavoidable for the conduct of scientifically valuable research." A study of pigs to understand how infant formulas affect human development is not scientifically valuable research when such research could be safely performed directly on humans. Soy-based formulas have been extensively studied in human infants, including their effects on sexual development. UAMS's animal use here is convoluted and at odds with the current standards of practice in human nutrition research in the United States.

Experimenters describe the study as "preclinical," reflecting their intention to apply the results to human clinical populations. Animals are not necessary for such research. As detailed below, soy-based infant formulas have been extensively studied in human clinical trials

2. UAMS' Justification of Animal Use Is Insufficient Because Alternatives Exist

Section 2143 of the Animal Welfare Act and C.F.R. Title 9, Section 2.31(d)(1)(i, ii) of the Animal Welfare Act's implementing regulations require that the principal investigator (PI) consider alternatives to procedures that may cause more than momentary or slight pain or distress to any animal used for research or educational purposes.

The PI did not meet this requirement because there is no rationale for animal use in human nutrition research given the abundance of human studies examining the estrogen effects of infant formulas. Having not provided objective evidence to support the use of animal subjects where study of human subjects is common, ethical, and more relevant to the stated research goals, the PI did not meet this requirement of the Animal Welfare Act.

A proper alternatives search would have revealed nonanimal methods for infant formula research and an abundance of peer-reviewed literature demonstrating the equivalence or superiority of human biology-based models compared to animal use. For example:

- A study compared reproductive organ volumes and structural characteristics in children at the age of five who were enrolled in the Beginnings study long-term cohort. In this study, breast bud, uterus, ovaries, prostate, and testes volumes and characteristics were assessed by ultrasonography in 101 children (50 boys and 51 girls) aged five who were breastfed or fed cow-milk formula or soy formula as infants. Analyses were adjusted for race, gestational age, and birth weight. The authors concluded that no early infant feeding effects were found on reproductive organ volumes and structural characteristics.[2]

- A study followed 147 male infants who were breastfed or fed cow-milk formula or fed soy formula for up to nine months. Using a combination of ultrasound imaging, blood tests, and noninvasive urogenital epithelial cell collection, the authors found no significant differences between boys fed cow-milk vs soy formula and that estradiol was not detectable.[3]

- A study of young adults fed soy formula for several months as infants found no evidence of hormonal or other adverse effects. In this case, over 811 subjects participated; 248 had received soy formula and 563 had received milk-based formulas during their first four months. No significant differences were found in general health and development between the two formula groups in either females or males.[4]

UAMS should not have used animals here. Given that soy infant formulas are already commercially and clinically used, the endpoints could have been studied in humans.

3. The Use of Animals for Infant Formula Research Is Duplicative and Not "Unavoidable"

Under the Animal Welfare Act, the investigator must assure the IACUC that "the activities do not unnecessarily duplicate previous experiments." C.F.R. § 2.31(d)(iii). Further, the PI must design activities involving animals to "assure that discomfort and pain to animals will be limited to that which is *unavoidable* for the conduct of scientifically valuable research." 9 C.F.R. § 2.31(e)(4).

The PI did not meet this requirement because numerous clinical trials have already studied and reported the effects of soy formula on estrogen and infant development. This clearly demonstrates that such use of live animals is not "unavoidable."

4. UAMS' IACUC Is Failing to Properly Oversee Animal Use

Section 2143 of the Animal Welfare Act and Title 9, Section 2.31(d)(1)(i, ii) of the Animal Welfare Act's implementing regulations require that the IACUC enforce the requirements described in items 1 through 3 above and thereby determine that the proposed activities are in accordance with the Animal Welfare Act and C.F.R Title 9, Section 2.31(d).

UAMS' IACUC failed this requirement by approving the animal use protocol despite the violations described in items 1 through 3, above. Thus, the Physicians Committee alleges inadequate oversight by UAMS' IACUC.

Accordingly, the Physicians Committee requests that APHIS investigate this matter and order corrective action and appropriate penalties.

Thank you for your attention.

Sincerely,

(b) (6)

Cc: (b) (6)
(b) (6) Jeff Wolchok, IACUC Chair, UAMS; Archie Tucker, Area Director, USDA Agricultural Research Services;

---

[1] Ronis MJJ, Gomez-Acevedo H, Shankar K, Hennings L, Sharma N, Blackburn ML, Miousse I, Dawson H, Chen C, Mercer KE, Badger TM. Soy Formula Is Not Estrogenic and Does Not Result in Reproductive Toxicity in Male Piglets: Results from a Controlled Feeding Study. *Nutrients*. 2022; 14(5):1126. https://doi.org/10.3390/nu14051126

[2] Andres A, Moore MB, Linam LE, Casey PH, Cleves MA, Badger TM. Compared with feeding infants breast milk or cow-milk formula, soy formula feeding does not affect subsequent reproductive organ size at 5 years of age. *J Nutr*. 2015;145(5):871-875. doi:10.3945/jn.114.206201

[3] Adgent MA, Umbach DM, Zemel BS, et al. A longitudinal study of estrogen-responsive tissues and hormone concentrations in infants fed soy formula. *J Clin Endocrinol Metab*. 2018;103(5):1899-1909. doi:10.1210/jc.2017-02249

[4] Strom BL, Schinnar R, Ziegler EE, Barnhart KT, Sammel, MD, Macones GA, et al. Exposure to soy-based formula in infancy and endocrinological and reproductive outcomes in young adulthood. *J. Am. Med. Assoc*. 2001:286:807–814.

McCoy, Devora (NIH/OD) [E]

From: Brown, Patricia [OLAW] (NIH/OD) [E]
Sent: Thursday, October 13, 2022 11:48 AM
To: (b) (6)
Cc: Deborah Dubow Press; Wolff, Axel (NIH/OD) [E]; (b) (6) (b) (7)(C) @uark.edu; robert.m.gibbens@aphis.usda.gov; (b) (6) laxmi.yeruva@usda.gov; archie.tucker@usda.gov; Morse, Brent (NIH/OD) [E]
Subject: RE: Use of Animals for Human Infant Nutrition Research at the University of Arkansas for Medical Sciences
Attachments: UAMS milk formula study APHIS and OLAW complaint 10.13.22.pdf; UAMS soy formula study APHIS complaint 10.13.22.pdf

Follow Up Flag: Follow up
Flag Status: Flagged

Dear (b) (6)

This is to acknowledge receipt of your letter concerning the University of Arkansas for Medical Sciences. At this time your concerns are under review.

Sincerely yours,

Patricia Brown, VMD, MS, DACLAM (she/her)
Director, Office of Laboratory Animal Welfare,
Office of Extramural Research,
Office of the Director, NIH
6700B Rockledge Drive
Bethesda, MD 20892-6910
301-496-7163
brownp@mail.nih.gov

From: (b) (6)
Sent: Thursday, October 13, 2022 7:47 AM
To: Brown, Patricia [OLAW] (NIH/OD) [E] <brownp@od.nih.gov>; robert.m.gibbens@aphis.usda.gov
Cc: (b) (6) Wolff, Axel (NIH/OD) [E] <wolffa@od.nih.gov>; (b) (6) (b) (7)(C) @uark.edu; (b) (6) laxmi.yeruva@usda.gov; archie.tucker@usda.gov
Subject: [EXTERNAL] Use of Animals for Human Infant Nutrition Research at the University of Arkansas for Medical Sciences

Dear Dr. Gibbens and Dr. Brown:

The Physicians Committee for Responsible Medicine requests that the United States Department of Agriculture's Animal and Plant Health Inspection Service and the National Institutes of Health's Office of Laboratory Animal Welfare investigate the University of Arkansas for Medical Sciences for the killing of piglets in two studies where experimental alternatives were readily available. As described in the attached letters, the use of animals here violates the Animal Welfare Act's mandate that experiments be "designed to assure that discomfort and pain to animals will be limited to that which is unavoidable for the conduct of scientifically valuable research." The use of animals here was neither scientifically valuable nor unavoidable.

The Physicians Committee requests that APHIS and OLAW investigate this matter and order correction and appropriate penalties.

Thank you for your attention.

Sincerely,