MARY FELZKOWSKI
STATE SENATOR • 12TH SENATE DISTRICT

Testimony on SB 894
Senator Mary Felzkowski
Committee on Government Operations, Legal Review and Consumer Protection
February 8, 2022 | 12:00pm | 201 Southeast

Chairman Stroebel and Fellow Members of the Committee:

Thank you for allowing me the opportunity to testify on Senate Bill 894, which would require the state government to show their proof, utilize feedback from impacted industries, and be held accountable for any scientific irregularities in promulgated or published rules that are based on, or rely on, scientific studies, scientific technical data, scientific methods, or other similar scientific information.

This bill is very simple – "follow the science."

Time and time again, we hear this phrase mentioned throughout the Capitol – here is an opportunity to put hyperbole aside and ensure that decisions being made for the state of Wisconsin fulfill our duty of creating sound, scientifically accurate policy.

Senate Bill 894 has three components to it:

The first allows for JCRAR or persons who may be regulated under a proposed rule to request an external peer review if they have an objection to specific studies or technical data; specific scientific methods; specific findings, conclusions, or assumptions that the agency used in developing the rule; or if they object on the basis that the rule does not comply with state or federal law.

The second requires an agency to solicit comments from industries and persons who may be regulated under the rule. Valid comments must be included in the original statement of scope that is sent to the Department of Administration and the Governor. This will inform the agency of any concerns that industry experts have and will give DOA and the Governor's office more transparency when thinking about whether these proposed rules will hold up to an external peer review process - potentially saving the state time and money.

The third would require the Department of Health Services, when recommending groundwater standards to the Department of Natural Resources, to publish on their website the following information: the proposed recommended enforcement standard; the scientific or technical data; the methodologies; and the findings, conclusions, and assumptions that the department used in developing that enforcement standard. If a person who may be regulated under the proposed standard objects to the science, DHS will be required to convene a working group of agency and

Capitol Office: P.O. Box 7882 • Madison, WI 53707-7882 • (608) 266-2509 • **Toll-Free:** (800) 334-8775
Cell: (715) 966-3366 • Sen.Felzkowski@legis.wi.gov

industry members to review the recommendation and decide whether or not it needs to be modified.

All in all, Senate Bill 894 is about transparency. We owe it to the people of Wisconsin to ensure that the science behind state regulation is based on data that is supported by the scientific community. Science has no room for partisan agenda, and this is a great first step in achieving sound, scientifically accurate policy.

I've attached an in-depth breakdown of this bill to my testimony for your reading pleasure.

Thank you again for giving me the opportunity to testify in support of Senate Bill 894, and we'd be happy to answer any questions following Representative Dallman's testimony.

Senate Bill 894
Peer Review Standards

Goal: Require the state government to show their proof, utilize feedback from impacted industries, and be held accountable for any scientific irregularities in promulgated or published rules that are based on or rely on scientific studies, scientific technical data, scientific methods, or other similar scientific information. The bill has three main components:

1. JCRAR and Impacted Party Request for a Peer Review
2. Industry Feedback in the Scope Statement
3. Requesting a Working Group on Proposed Groundwater Standards

Who can request a peer review, and when:

- **JCRAR** - can request an external peer review of a rule being promulgated by an agency any time prior to the proposed rule being submitted to the Governor for approval. JCRAR can also request a peer review of any rules published in the administrative code. A request for a peer review by JCRAR is considered valid if it objects to specific studies or technical data; specific scientific methods; specific findings, conclusions, or assumptions that the agency used in developing the rule; or if it objects on the basis that the rule does not comply with state or federal law. JCRAR cannot object to a rule that has previously been the subject of an external peer review.
- **Interested Parties** - Defined as a person who will be regulated under a proposed rule, or a person whose client, member, or customer will be regulated under a proposed rule. An interested party can request an external peer review of a rule being promulgated by an agency any time prior to the proposed rule being submitted to the Governor. A request for a peer review by an interested party is considered valid if it objects to specific studies or technical data; specific scientific methods; specific findings, conclusions, or assumptions that the agency used in developing the rule; or if it objects on the basis that the rule does not comply with state or federal law. An interested party cannot object to a rule that has previously been the subject of an external peer review.

Upon receiving a valid request for a peer review, an agency has 60 days to contract with the National Academy of Sciences, Toxicology Excellence for Risk Assessment, any similar independent scientific entity, or with a group of independent scientists of comparable stature and qualifications, to conduct an external peer review. The peer review shall be completed within six months, but can be extended for another six months if necessary.

The peer review panel will submit a written report to the agency with one of the following determinations, *and resulting action*:

- The rule is scientifically defensible - *the agency may continue promulgating the proposed rule and the objecting party pays for the peer review*

- The rule is not scientifically defensible - *the agency shall initiate the rule-making process to make necessary modifications and the agency pays for the peer review*
- The rule would be scientifically defensible if the agency made certain specified modifications - *the agency, before continuing the to promulgate the rule, must work in cooperation and agreement with the objecting party to make necessary modifications and the agency pays for the peer review*

Industry feedback in the scope statement:

Prior to an agency sending a statement of scope to the Department of Administration and the Governor, they must solicit comments from industries and persons who may be regulated under the rule. Any valid comments for rules that are based on or rely on scientific studies, scientific or technical data, scientific methods, or other similar scientific information must be included in the statement of scope. This will inform the agency of any concerns that industry experts have and will give DOA and the Governor's office more transparency when thinking about whether these proposed rules will hold up to an external peer review process - saving the state any potential unnecessary time and money.

Groundwater Standards Working Groups:

Prior to the Department of Health Services submitting a groundwater standards recommendation to the Department of Natural Resources, DHS must provide public notice of the developed standard. The notice must be published on the DHS website, including the proposed recommended enforcement standard; the scientific or technical data; the methodologies; and the findings, conclusions, and assumptions that the department used in developing that enforcement standard.

If an interested party objects to a recommendation based on the accuracy, integrity, objectivity, or consistency of the data used in the development process, DHS must convene a working group along with the following members to review the recommendation:

- Interested party
- Four members from statewide agriculture associations
- One member from DATCP
- One member from DNR

If there is a consensus by the working group that changes are needed to ensure the accuracy, integrity, objectivity, or consistency of the data used to develop the recommendation, DHS shall modify the recommendation accordingly before submitting it to the DNR.

ALEX A. DALLMAN

STATE REPRESENTATIVE • 41ST ASSEMBLY DISTRICT

Testimony in favor of Senate Bill 894

Senate Committee on Government Operations, Legal Review and Consumer Protection

February 8th, 2022

Thank you, Chairman Stroebel and committee members, for allowing me to testify before you concerning Senate Bill 894, relating to the peer review of administrative rules. I would also like to thank Senator Felzkowski for her leadership on this legislation.

This bill would create a much needed, external, peer review process for administrative rules that are based on scientific studies. Current law provides important opportunities for the public to engage in the rulemaking process, however, there is an ongoing issue with the lack of an independent, peer review of agency standards that are based on scientific studies.

Senate Bill 894 would address the following items:

- Requires an agency to assemble an external peer review process of a prospective rule upon request by an affected party
- Requires an agency to promote and incorporate scientifically valid comments from affected parties into scope statement
- Rebuilds the process for recommending groundwater standards, including providing public notice of prospective recommendations by DHS prior to submittal to DNR

We often all hear the slogan, "follow the science". I believe I can speak for both Senator Felzkowski and myself in that we both agree that our bureaucracy should be "following the science" when it promulgates new rules and adds more red tape onto the backs of our local business men and women. This bill simply asks to back up new policy with facts based in science and studies – not feelings and opinions. Sound governance for all Wisconsinites will derive from scientifically based policy.

Thank you again, Chairman Stroebel, for the opportunity to testify before this committee today and I would be happy to answer any questions you may have.

P.O. Box 8952 • Madison, WI 53708-8952 • (608) 266-8077 • Toll-Free (888) 534-0041 • Fax: (608) 282-3641
Rep.Dallman@legis.wi.gov

Wisconsin Conservation Voters

Testimony in Opposition to SB 894
Peter Burress, Government Affairs Manager
February 8, 2022

Good afternoon Chair Stroebel and members of the committee. My name is Peter Burress. I am the Government Affairs Manager with Wisconsin Conservation Voters. We have offices in Madison, Milwaukee, and Green Bay, where we work with our network of over 40,000 members and supporters to engage voters to protect our environment. I appreciate the opportunity to testify in opposition to Senate Bill 894, which threatens the health of Wisconsin communities by adding delays to administrative rulemaking, corrupting the scientific foundations of the process, and prioritizing the voices of polluters over those of impacted people.

It takes 30 months to establish a new public health standard.[1] Senate Bill 894 allows polluters to grind this process to a halt by objecting to agency recommendations and requesting a biased external peer review. This makes an already-lengthy process even longer, and comes at a moment when Wisconsinites cannot afford to wait any longer for baseline public health protections. One example of this relates to the impact that PFAS are having on our communities.

PFAS are a class of highly toxic, human-made chemicals that have been tied to increased rates of testicular and kidney cancer. Exposure can also lead to increased cholesterol levels, liver damage, decreases in infant birth weights, and increased risk of high blood pressure in pregnant women.[2] Currently, the DNR is working to finalize standards for two PFAS chemicals. With PFAS-related threats facing Wisconsinites in Campbell, La Crosse, Madison, Eau Claire, Rib Mountain, Rhinelander, Peshtigo, Marinette, and others, we know that any biased procedural delays mean more testicular cancer, more heart disease, and more sick infants.

Supporters of Senate Bill 894 may suggest the bill adds science-based review processes for new standards. We know that our health depends on sound science, but the details of this bill do not support sound science. The bill states that, "Peer review questions and protocols shall be approved, prior to use in the peer review, by the agency *and any parties requesting the peer review*." This gives polluters too much control over what the process should look like – a dangerous conflict of interest that corrupts our agency commitments to balanced, unbiased science.

One example of this commitment is the DNR's Cycle 10 rulemaking process, which would add new state groundwater quality standards for 17 substances including two PFAS chemicals.[3] This is a tested process that has already been used to set public health-based

[1] https://legis.wisconsin.gov/lc/media/1597/20adminrules_manual.pdf
[2] https://www.atsdr.cdc.gov/pfas/health-effects/index.html
[3] https://dnr.wisconsin.gov/sites/default/files/topic/Rules/DG1519DraftRule2.pdf

groundwater quality standards for 138 chemicals in Wisconsin – including arsenic, mercury, and PCBs.[4]

Within this rigorous process, DHS developed recommended standards based on relevant scientific information from the Environmental Protection Agency, the Agency for Toxic Substances and Disease Registry, and the World Health Organization. It also screened 8,900 peer-reviewed scientific studies,[5] culminating in a 328-page scientific support document.[6] Senate Bill 894 corrupts this process by allowing polluters to stop agency work so they can drive a biased, lengthy external review.

Finally, Senate Bill 894's supporters may also suggest that the proposed external review provides an opportunity for regulated parties to be heard. However, throughout the rulemaking process, there are already six formal opportunities where all interested parties can provide input.[7] In its most recent public comment period on the Cycle 10 rulemaking, the DNR received 421 pages of comments, the vast majority of which were very supportive.[8] Senate Bill 894 creates a separate process for influencing standards that would exclude most impacted members of the public.

To protect the health and safety of every Wisconsinite, we need unbiased, science-based processes that quickly provide protections for people, not polluters. Senate Bill 894 delays protections, corrupts science-based processes, and excludes impacted Wisconsinites. We therefore ask you to oppose it.

Thank you for your time.

###

For more information, contact Peter Burress at peter@conservationvoters.org or 920-421-3601. Visit Wisconsin Conservation Voters at www.conservationvoters.org.

[4] https://dnr.wisconsin.gov/topic/Groundwater/CurrentStandards.html#health
[5] https://dnrmedia.wi.gov/main/Play/9f8f56142a2e4232b97d9df7523444d81d?catalog=9da0bb432fd448a69d86756192a62f1721 (skip to 1:35)
[6] https://www.dhs.wisconsin.gov/publications/p02434v.pdf
[7] https://dnrmedia.wi.gov/main/Play/9f8f56142a2e4232b97d9df7523444d81d?catalog=9da0bb432fd448a69d86756192a62f1721 (skip to 1:35)
[8] https://widnr.widen.net/view/pdf/cm1gwvg72q/DG_DG1519_WrittenComments.pdf?t.download=true

WMC
Wisconsin's Chamber

TO: Members, Senate Committee on Government Operations, Legal Review & Consumer Protection

FROM: Craig Summerfield, Director of Environmental & Energy Policy, WMC

DATE: February 8, 2022

RE: Support for Senate Bill 894 – Peer Review of Administrative Rules

Wisconsin Manufacturers & Commerce (WMC) appreciates the opportunity to testify in support of Senate Bill 894. We sincerely thank the authors – Senator Felzkowski and Representative Dallman – for bringing this important legislation forward. This bill creates a much-needed peer review process for administrative rules that are based on scientific studies.

WMC is the largest general business association in Wisconsin, representing approximately 3,800 member companies of all sizes, and from every sector of the economy. Since 1911, our mission has been to make Wisconsin the most competitive state in the nation to do business. That mission includes advocating for predictable regulatory standards for the business community that are based on sound science.

Thanks to key reforms by Wisconsin lawmakers, current law provides important opportunities for the public to engage in the rulemaking process. For example, 2017 WI Act 57 – otherwise known as the REINS Act – provides a mechanism to require agencies to hold a public hearing earlier in the rulemaking process, and requires a legislative vote on expensive rules that trigger more than $10 million in compliance costs over any two year period. These changes allow the public to engage in the rulemaking process earlier and provide an additional layer of transparency for very expensive bureaucratic rules.

Senate Bill 894 builds on past rulemaking reforms by creating a peer review process for administrative rules. To begin, it is important to clarify that current law does not provide for a peer review process for proposed state standards. An agency may review relevant scientific studies when recommending a standard, and this may include a search of peer-reviewed studies. However, this is simply not the same as subjecting the recommendations *themselves* to peer review.

In addition, opponents have suggested that this bill is unnecessary because of existing opportunities for public comment. However, there are two key problems with this claim. First, under current law there is no public comment opportunity while groundwater standards are developed by the Wisconsin Department of Health Services (DHS). After DHS groundwater recommendations are made, the agency simply forwards these standards to the Department of Natural Resources in order to promulgate rules.

MWFPA
Midwest Food Products Association, Inc.

TO: **Members**
Wisconsin Committee on Senate Operations, Legal Review and Consumer Protection

FROM: **Jason Culotta**
President
Midwest Food Products Association

DATE: **February 8, 2022**

RE: **Support for Senate Bill 894 – Peer Review of Proposed Groundwater Standards**

The Midwest Food Products Association (MWFPA) represents food processing companies operating in Illinois, Minnesota, and Wisconsin. Our members produce a variety of food products which feed the national, particularly canned and frozen vegetables. Using science-based standards for setting groundwater standards is particularly important for the processing industry.

We would like to thank Senator Felzkowski and Rep. Dallman for authoring Senate Bill 894, which would allow a peer review process for certain instances where a proposed groundwater standard can be challenged for lack of scientific basis.

Wisconsin has long used a process where the Department of Health Services (DHS) proposes groundwater standards and the Department of Natural Resources (DNR) promulgates those standards in an administrative rule under Chapter 160/NR 140 – without deviation.

The challenge to this process occurs when DHS must consider what an appropriate standard is, the agency does not consistently rely on published scientific data and may end up with an extraordinarily low threshold that effectively removes a crop treatment from use. Wisconsin is presently in Cycles 10 and 11 of this process to determine groundwater standards under the Chapter 160/NR 140 process.

SB 894 creates an avenue for independent peer review of agency standards based on scientific studies and would positively impact accurate groundwater standards governed by Chapter 160. Similar language has long been in place in California and Idaho. The costs of conducting the peer review of a proposed standard to a substance that is challenged would be paid by the prevailing party.

Water is an essential ingredient for the agriculture and food industries. Food manufacturers use water in many products but also to clean, peel, heat, and steam raw products. We support efforts to manage and ensure access to clean, healthy water – including groundwater – yet also recognize the need to proceed deliberately to ensure new regulations accurately address challenges where they exist.

As the voice of food manufacturers, the Midwest Food Products Association (MWFPA) has seen this situation arise over time. Acting on DHS' recommendation, DNR adopted a very strict limit for the corn herbicide alachlor in 2005 during Cycle 8. The Joint Committee for Review of Administrative Rules requested that this proposed standard have an external, independent, and unbiased scientific peer review. DNR rejected this recommendation and the very low standard for alachlor was adopted in 2007.

In Cycle 10, the proposed groundwater standard for the substance imidacloprid was set lower than the guidelines recommended by national experts. This crop management tool is used widely in agriculture across Wisconsin and the proposed standard, set ultra-low, will likely remove this tool from the industry's toolbox. Outside parties are not given an opportunity to have input on the proposed regulation of these substances when developed by DHS and an outside peer review of the process is not presently an option.

Also in Cycle 10, the proposed standard for glyphosate – the primary substance in Roundup – made the Chapter 160/NR 140 list for the first time. While it is not inappropriate to set a standard for the use of this substance, the proposed standard is set so low that its use will be extremely restricted in the state once the final rule is approved.

We ask that you consider approving SB 894 to allow the opportunity for a peer review process to be selectively and independently used to help the agencies consistently arrive at a science-based decision on setting these crucial standards.

State of Wisconsin
DEPARTMENT OF NATURAL RESOURCES
101 S. Webster Street
Box 7921
Madison WI 53707-7921

Tony Evers, Governor
Preston D. Cole, Secretary
Telephone 608-266-2621
Toll Free 1-888-936-7463
TTY Access via relay - 711

Senate Committee on Government Operations, Legal Review and Consumer Protection

2021 Senate Bill 894
Peer Review of Administrative Rules, Comments to Proposed Statements of Scope, and Review of Proposed Groundwater Enforcement Standards

February 8, 2022

The Wisconsin Department of Natural Resources (DNR) welcomes the opportunity to provide written testimony on Senate Bill 894, related to peer review of administrative rules, comments to proposed statements of scope, and review of proposed groundwater enforcement standards.

The Department of Natural Resources follows a scientifically sound peer review process when promulgating science-based rules. This bill would add a step in the rulemaking process that gives private individuals and interest groups an unprecedented role that would undermine the scientific process.

The scientific peer review process is simple: a scientist studies something and documents the result or conclusion; other scientists review it and provide feedback; the scientist considers the comments and revises their work based on the feedback. Current law and agency practice provide for neutral scientific review of proposed rules by scientists who engage in and rely on the peer review process. There are ample opportunities in the rulemaking process for input from all interested parties on the science that forms the basis for DNR rules. The rulemaking process includes public comment during the preliminary scope hearing, economic impact analysis solicitation period, and the proposed rule hearing and public comment period. Additional opportunities for comment are provided for DNR rules as part of the Natural Resources Board review and approval process. Under current law, the department reviews and responds to all comments received relating to the scientific basis for a proposed rule.

The current scientific peer review process works. The department regularly receives detailed critique of proposed rules from scientists and scientific organizations. The agency scientists review and consider this feedback and revise the rule as necessary, including changing standards in light of scientific information raised during the public comment process. This is scientific peer review.

This bill would not create a true scientific peer review process. Rather, it would empower any member of the regulated community – regardless of whether they have any scientific training or background – to approve the peer review questions and protocols for a process that determines the fate of the rule in question. The bill's external peer review could be demanded at any stage of rulemaking, including before the agency scientists have an opportunity to complete their review of public comments and input from the scientific community. In short, this bill intrudes upon and undermines the current scientific peer review process.

The outcome of the process outlined in this bill would be a determination, made by group of private citizens, of two things: scientific defensibility and consistency with state and federal law. Regarding

scientific defensibility, the bill contains no standard or definition for the term, and it has no generally understood meaning in the scientific community. Regarding a determination of consistency with state and federal law, it is inappropriate to task a panel of private citizen scientists with determining the legality of a rule. That task cannot and should not be delegated to a panel of private citizens – even if those citizens have a scientific expertise.

This bill would create a process that could result in conflicting and confusing results. This would not improve the scientific integrity of the process. The bill requires that an agency adopt any scientifically valid comments into its scope statement, which could mean that the agency would be required to incorporate multiple, conflicting comments, or comments that are contrary to the agency's policy decisions. It would allow private citizens the authority to potentially come to a scientific result that is contrary to federal- or state-mandated standards.

We frequently hear from the public and the regulated community that the rules process is too difficult to follow, too complicated, and often that they are confused by what public comment period relates to what part of the process. Further complicating the public comment requirements at the scope statement phase and adding a potential peer review panel report to any rulemaking process would only make it harder for all interested stakeholders and members of the public to meaningfully engage in the rulemaking process.

Additionally, the bill allows a private citizen or interest group to demand the agency engage in this external peer review process; but the private citizen or interest group must pay for the peer review if the peer review panel determines that the proposed rule is scientifically defensible. This means that only private citizens and interest groups that have sufficient funds to commit to paying an undefined amount of money for the study could make such a request. This puts the power to engage in this proposed process in the hands of only the wealthiest in our state.

Briefly, we would like to turn to the provisions of this bill that pertain to ch. 160, Wis. Stat. governing groundwater standards. The bill adds a provision requiring the Department of Health Services (DHS) to convene a working group if anyone submits a written objection to DHS groundwater recommendations before the recommendations are provided to DNR. DHS recommendations are already subject to several rounds of public comment during the DNR rulemaking process, during which the scientists at both agencies often agree to make changes to the standards in light of scientific information submitted during the public comment period. Additionally, the composition and function of the working group is unclear and not functional, with no process, requirements, end product, meeting requirements, or timeline identified for a working group that could potentially include an unlimited number of private citizens and interest groups.

In conclusion, this bill is duplicative, unnecessary, expensive, and interferes substantially with the scientific process and the agency's ability to regulate the state's natural resources. Residents in communities across the state are calling for action on issues like PFAS, and the legislature should be working to advance the CLEAR Act and other meaningful solutions to environmental contamination rather than creating barriers to progress within a process driven by science and shaped by public input.

Thank you for the opportunity to provide this written testimony. If you have questions or if there is any further information the department can provide, please feel free to contact Sean Kennedy, DNR Legislative Director, at Seanp.Kennedy@Wisconsin.gov.

State of Wisconsin
Department of Health Services
Tony Evers, Governor
Karen E. Timberlake, Secretary-Designee

TO: Members of the Senate Committee on Government Operations, Legal Review, and Consumer Protection

FROM: HJ Waukau, Legislative Director

DATE: February 8, 2022

RE: Senate Bill 894, relating to: peer review of administrative rules, comments to proposed statements of scope, and review of proposed groundwater enforcement standards

The Wisconsin Department of Health Services (DHS) would like to thank the Committee for the opportunity to submit testimony for information only on Senate Bill 894 (SB 894), regarding the peer review of administrative rules. SB 894 would create an external peer review process for the state's administrative rules that are based on scientific studies, methods, data, or information. Under the bill an interested party may request an external peer review of a proposed rule at any time before it is submitted to the Governor for review, for example during the creation of a statement of scope. The Joint Committee for Review of Administrative Rules (JCRAR) would also be able to request an external peer review of any existing or proposed administrative rule. SB 894 provides provisions for what may be considered a valid request for peer review and lays out the process for a peer review to be conducted and who is responsible for covering the costs of the review. Lastly, SB 894 creates new processes for DHS and the Department of Natural Resources (DNR) to follow regarding the development of groundwater standards.

Existing rule promulgation processes & considerations
Under Wis. Stat. § 227.19 (1)(b) the Legislature delegates its authority to administrative agencies in order to "eliminate the necessity of establishing every administrative aspect of general public policy by legislation." Accordingly, the Legislature has "the right and responsibility to designate the method for rule promulgation, review, and modification," and "the right to delay or suspend implementation of any rule or proposed rule while under review by the legislature," per Wis. Stat. § 227.19(1)(b)3. & 4, respectively. Further, agencies are prohibited from performing "any activity in connection with the drafting of a proposed rule, except for any activity necessary to prepare the statement of scope of the proposed rule until the governor and the individual with policy-making powers over the subject matter of the proposed rule approves the statement [of scope]." Per Wis. Stat. § 227.135(3) and 227.136(1) the Secretary of DHS is the individual with policymaking powers for the agency and they can't approve a statement of scope until after it has been published in the Administrative Register and there has been an opportunity for public comment and a preliminary public hearing (if requested by JCRAR or held on the agency's own accord). Under Wis. Stat. § 227.136(5), if any comments are offered during those periods, the agency is directed to consider those comments, revise the scope as necessary, and then move forward with statutorily-mandated processes for rule promulgation.

A statement of scope for all intents and purposes is a statement of policy and intention, and it does not contain detailed policy proposals or specific rule provisions. Per Wis. Stat. § 227.135(2), actual rule development can't occur until the scope has undergone publication and commenting requirements. The process proposed in SB 894 regarding a mandatory public comment period prior to submitting a scope to the Governor for approval under Wis. Stat. § 227.135(2) is duplicative of existing processes in Wis. Stat. § 227.135 and 227.136. It would also increase the amount of time needed to promulgate or amend a rule. Further, permitting public comments from "any person who may be regulated" and requiring the agency to consider those comments could venture into territory where the agency is considering specific policies or rule provisions that should only be considered after the Secretary has approved the rule following the requisite publication and comment periods. Such a process could be in violation of Wis. Stat. § 227.135(2).

Additionally, the provisions in SB 894 that would govern the external peer review of rules that have already been promulgated may fall outside of the Legislature's authority under Wis. Stat. § 227.19. Wis. Stat. § 227.26, relating to the review of rules after promulgation is the current framework to authorize the review or reopening of a previously promulgated rule. Under this process, and according to the Supreme Court of Wisconsin's holding in *Martinez v. DILHR*, the Legislature must comply with the process of presenting a bill to amend or repeal a rule under Wis. Stat. § 227.26(2)(f) and (h). SB 894 would allow JCRAR to request an external peer review of any previously promulgated rule and, if the external peer reviewers conclude that a rule is not defensible, then the agency would be required to initiate the rulemaking process to make modifications to the code as necessary. Such a process may conflict with the holding in *Martinez*, as it bypasses the existing statutory requirement under Wis. Stat. § 227.26 that JCRAR, following a complaint and holding a hearing, vote to take certain actions with respect to an already promulgated rule. After which JCRAR must then introduce a bill that must pass both houses of the legislature and be signed into law by the Governor.

The provisions of SB 894 would also have implications for the promulgation of emergency rules. If an external peer review is requested on a proposed rule which has a corresponding emergency rule, the six month external peer review process would take up most of the effective period of the emergency rule. While the provisions of SB 894 do allow for a pause on the 30-month timeframe for the promulgation of a permanent rule, it does not appear to make the same accommodation for an emergency rule. This oversight could inhibit DHS's capacity to respond to emergent threats to the health, safety, and welfare of the public as a permanent rule might not be promulgated before expiration of an emergency rule.

Implications for the creation of groundwater standards

The current process for the development of the state's groundwater standards are laid out in Chapter 160 of the state statutes. Per Wis. Stat. § 160, DHS develops recommendations for groundwater enforcement standards and DNR uses these recommendations to propose regulations for groundwater enforcement. DHS recommendations are based on existing federal standards and guidelines, peer-reviewed scientific studies, and information from scientific reviews conducted by federal agencies such as the Environmental Protection Agency (EPA) and the Agency for Toxic Substances and Disease Registry (ATSDR). Further, DHS assesses scientific studies to determine if they were conducted using scientifically valid protocols, characterize toxic effects relevant to human health, and are consistent with other credible medical or toxicological evidence. DHS recommendations to DNR are publicly available, and any party has the ability to provide comments on the standards at any time, including but not limited to, formal public hearing and comment periods. DHS and DNR consider and respond to any and all input received from the public which can result in promulgated groundwater standards that are different from the original DHS recommendation.

Similar to processes described above, the provisions of SB 894 are duplicative of current processes. Per SB 894 DHS must provide public notice of proposed recommended enforcement standards as well as the supporting scientific documents before transmitting information to DHS. This information is already made public at the time the recommendations are sent to DNR. The proposed workgroup as laid out by SB 894 is also duplicative of existing public input opportunities and creates redundant review processes specific to groundwater standards. Adding the creation of another workgroup would create significant delays in rule promulgation and have potentially serious impacts for public health protection. As described above the current process already allows for multiple opportunities for the public to engage in how the state develops its groundwater standards. Further, nothing precludes interested parties from objections to an already modified recommendation, which would result in DHS convening workgroups serially for a substance.

Additionally, the composition of the proposed workgroup for groundwater standards under SB 894 may not be appropriate for all standards. SB 894 would require DHS to convene a workgroup if an interested party objects to a proposed groundwater standard prior to the promulgation of said standard, based on a failure to comply with state groundwater laws or regarding the accuracy, integrity, objectivity, or consistency of the data used to develop the recommendation. The proposed workgroup would be composed of: the interested party; four members from state agriculture associations; one member from the Department of Agriculture, Trade, and Consumer Protection; and one member from DNR. While some groundwater standards have significant implications for agriculture not

all groundwater standards have agricultural implications. Many standards are for substances associated with other industrial activities such as metals and various organic chemicals. It is unclear at this time how the proposed workgroup would be able to provide appropriate recommendations on non-agricultural related standards given the proposed composition of the workgroup under SB 894.

Additional Considerations

Aside from the groundwater standards specified by SB 894 numerous other standards and regulations for DHS would be impacted by the bill. For example, SB 894 as written would impede and weaken Wisconsin's autonomy to administer certain federally delegated programs such as radiation protection. The publications referenced for radiation protection standards in Wis. Admin. Code ch. DHS 157, have already undergone a rigorous peer review process before adoption as a national or international standard. Public and occupational radiation dose limits are based on the source data produced by the National Academy of Sciences. That data is used by the National Council on Radiation Protection and Measurement and federal and state agencies to recommend standards for adoption into administrative rules. In this example SB 894 would require a reproduction of a peer-review process that has already occurred and specifically in relation to consultation and evaluation by the National Academy of Sciences. Similar peer-review process and consultations are repeated across DHS for rules and regulations relating to lead abatement, environmental standards, immunizations, and provider health and safety, just to name a few.

Lastly, the increase in regulatory requirements put forward by SB 849, particularly the peer review requirements, would increase DHS' workload and necessitate the hiring of new employees to be able to appropriately comply with the provisions of the bill. Further, DHS would incur additional costs from being required to contract with the National Academy of Sciences for the purposes of peer review. While the ultimate attribution of costs will not be known until a peer review is completed there will still be an initial cost to DHS for the purposes of procuring the contract, including staff time and resources to manage and track the peer review. SB 894 does not provide for any staffing authority or appropriations to administer the processes laid out in the bill, and these costs can't be absorbed under DHS' current operating budget.

DHS thanks the Committee for the opportunity to provide testimony for information only and offers its services as resource for the Committee.

Survival
Coalition
of Wisconsin Disability Organizations
P.O. Box [illegible], Madison, Wisconsin 53707

February 8, 2022

Senate Government Operations, Legal Review & Consumer Protection
Senator Stroebel, Chair
State Capitol, Rm 18 S
Madison, WI 53707

Dear Senator Stroebel and members of the committee:

Survival Coalition is concerned that the provisions within SB 894 related to setting groundwater enforcement standards for certain substances of public health concern will unnecessarily expose citizens to substances that cause chronic conditions and permanent disability.

There are currently 130 substances for which DHS has groundwater enforcement standards. Many of these regulated substances—including lead and mercury—have a known correlation or direct causal relationship to neurological delays, permanent disability, chronic health conditions, and preventable intellectual and developmental disabilities. Survival Coalition is concerned this bill would unnecessarily put children and families at risk of higher levels of exposure to substances with known negative health impacts. Survival Coalition is equally concerned that if additional substances are discovered to have a public health impact it would be more difficult to add them to the groundwater enforcement standards.

The methodology outlined in Wis. Stats. 160.13 to develop groundwater enforcement standards is highly detailed to ensure those standards are established in accordance with known science. The criteria are heavily focused on level of harm—including organ damage, severity of injury, cumulative effects of exposure, chronic effects of exposure, irreversibility, and physiologic or pathologic states and functional abnormalities that result from exposure.

The peer review process outlined in the bill significantly delays establishment of water quality standards protective of drinking water supplies and public health. It appears there is no limit to the number of peer reviews that can be requested or the number of times a party can trigger peer review, creating a s seemingly open-ended process that could indefinitely prevent substances with known health impacts from being regulated as long as there are entities willing to pay for reviews. SB 894 is overly vague on what "consensus" means, and what happens if "changes" do not satisfy the objector.

The peer review process envisioned by this bill is weighted towards interests with an incentive to prevent or reduce regulation and avoid remediation or liability for contaminated water. However, individual citizens who are at risk or may have already suffered harm and advocates concerned with these issues are denied a similar ability to initiate a peer review.

Delays in implementing groundwater enforcement standards caused by multiple peer reviews may serve to add to the number of people diagnosed with disabilities because during these delays additional people may become acutely and chronically ill or disabled from ingesting dangerous substances that the peer review process has kept unregulated or under regulated.

As the legislature can direct promulgation of admin rules and JCRAR already has significant authority to scrutinize and require changes, we do not believe the extra layer of peer review proposed by the bill is necessary.

Survival Coalition is comprised of more than 20 statewide disability organizations, and has members with expertise in disability law, research and best practices, and providing direct services for people with disabilities.

Thank you for your consideration of these important concerns,

Survival Co-Chairs:

Beth Swedeen, beth.swedeen@wisconsin.gov; (608) 220-2924;
Kristin M. Kerschensteiner, kitk@drwi.org; (608) 267-0214;
Patti Becker, beckerp@clanet.org; (608) 242-8335

Senate Committee on Government Operations, Legal Review and Consumer Protection
Testimony in Support of SB 894
February 8, 2022

Chairman Stroebel, Vice-Chair Felzkowski and committee members,

Thank you for the opportunity to provide testimony in support of Senate Bill 894.

We first want to thank the authors of SB 894 for tackling such a complex regulatory process and greatly improving upon it with this common-sense bill that increases regulatory transparency by allowing for increased scientific review and public input. Wisconsin's farmers thank you.

Wisconsin Dairy Alliance (WDA) represents modern regulated dairy farms in Wisconsin and works diligently to preserve Wisconsin's heritage as the Dairy State. **Venture Dairy Cooperative (VDC)** works to combat unnecessary regulations, reduce government bureaucracy and advance smart policy to support the future of dairy farmers.

Farmers are some of the most responsible conservationists of our land in the state. Wisconsin farmers, and especially large producers, work consistently to lower their environmental footprint through improved farming practices, and heard and nutrient management. The ability of farmers to continue to efficiently feed the world is compromised when regulatory agencies regulate behind closed doors, as they do currently when establishing groundwater standards.

Our members rely on clean water and soil. We want clean water too. CAFOs are held to the highest standards as it relates to managing nutrients. They must abide by Nutrient Management Plans and are audited annually by the DNR to ensure they are compliant. CAFOs are already subject to a zero-discharge standard per the terms of their stringent Wisconsin Pollutant Discharge Elimination System (WPDES) permit.

Because they are so highly regulated, our farmers rely on regulatory certainty, predictability, and on the opportunity to participate in the regulatory process.

Currently, Wisconsin establishes its groundwater standards through a multi-step Department of Health Services (DHS) and the Department of Natural Resources (DNR). DHS develops a recommended groundwater standard for compounds requested by the DNR. *The development of recommendations at DHS happens without any oversight or opportunities for public or outside, scientific review.*

Then, DNR simply accepts these proposed standards and moves forward with its regulations based on that standard. Under the current process, then, the most impactful portion of establishing

groundwater regulations is done without oversight. This can result in groundwater standards that do not use the best available science. This is why this bill is so important and why this bill must become law.

This bill requires a peer review of a proposed rule when an affected party makes the request and requires an agency to solicit scientifically valid comments from affected parties into a scope statement. Finally, it reforms the process for recommending groundwater standards, including providing public notice of proposed recommendations by DHS prior to submittal to DNR. It increases transparency, bolsters the science behind the standards, and enhances accountability.

Nothing about this bill prevents DNR and DHS from protecting groundwater. Rather, it simply allows for opportunity for review of scientists and input from the public. It increases transparency of agency action and expands opportunities for input from the experts. It is difficult to imagine why anyone who supports transparency in regulation would oppose such legislation and look forward to it garnering bipartisan support.

Thank you again for the opportunity to submit this testimony and thank you to the authors for standing with Wisconsin's farmers.

Sincerely,

Kim Bremmer- Venture Dairy Cooperative

Cindy Leitner- Wisconsin Dairy Alliance

For more information please Contact Lane Ruhland at lane@ruhlandlaw.com

Eastern Research Group, Inc.

June 25, 1999

Environmental Science and Engineering

Economic and Regulatory Analysis

Environmental and Occupational Health Services

Software Applications Development

Pollution Prevention

Technology Evaluation

Environmental Sampling and Analysis

Technical Writing and Editing

Meeting Management and Facilitation

Graphic Design and Media Services

Public Relations and Outreach

Education and Training

Steve Karklins
Wisconsin Division of Health
Bureau of Drinking Water and Groundwater
101 South Webster Street
Box 7921
Madison, WI 53707-7921

Dear Steve,

As you know, over the past few months ERG has been coordinating the independent scientific and technical peer review of the draft document entitled "Recommendation for an Enforcement Standard and a Preventive Action Limit for Ammonia in Groundwater." After receiving this draft document from the Wisconsin Department of Natural Resources, ERG reviewed the document and then identified three nationally recognized scientists with the appropriate expertise to serve as peer reviewers. We also discussed any potential conflicts of interest with the peer reviewers, and determined that no conflicts existed. The three reviewers for the draft document are:

Dr. Herbert Cornish
Private Consultant - Formerly of the University of Michigan
830 W. Clark Road
Ypsilanti, MI 48198

Dr. Arthur Gregory
Private Consultant and President - Techto Enterprises
1 Gregory Lane
Luray, VA 22835

Dr. James Withey
Private Consultant - Formerly of Health Canada
49 Wilton Crescent
Ottawa, Ontario K1S-2T6
Canada

Corporate Headquarters:
110 Hartwell Avenue
Lexington, MA 02421-3134
Phone 781-674-7200
Fax 781-674-2851

2200 Wilson Boulevard
Suite 400
Arlington, VA 22201-3324
Phone 703-841-0500
Fax 703-841-1440

14555 Avion Parkway
Suite 200
Chantilly, VA 20151-1102
Phone 703-633-1600
Fax 703-263-7286

900 Perimeter Park (Lab)
P.O. Box 2010
Morrisville, NC 27560-2010
Phone 919-468-7800
Fax 919-468-7803

1600 Perimeter Park (Office)
P.O. Box 2010
Morrisville, NC 27560-2010
Phone 919-468-7800
Fax 919-468-7801

We sent each reviewer a copy of the document to be reviewed, as well as the list of 8 questions to be addressed in the review, which we received from you. These questions were intended as a guide for the consultants in performing their review. In addition, we sent each peer reviewer a conflict of interest certification to sign.

We asked the peer reviewers to provide a written summary of their comments on the document, focusing on the 8 questions. We also instructed the peer reviewers to annotate pages from the draft document, and to include any additional references they may have cited in their review. Attached are the completed peer reviews.

If you have any questions, or require any additional information, please do not hesitate to contact me at 781-674-7323. It has been a pleasure to work with you.

Sincerely,

Heidi Schultz
Coordinator

PEER REVIEW COMMENTS
FROM

HERBERT CORNISH

Nicole Schubert
Peer Review Coordinator
Eastern Research Group
110 Hartwell Avenue
Lexington, MA 02421-3134

June 24,1999

Dear Nicole:
I think I'm going to get this in just before the deadline. I must admit I spent a great deal of time on this document. It's the first document I have reviewed which I think was not very well done.

Their choice for basing their calculation on the dose level for an old medicine did not seem appropriate to me. I have suggested that some of the new data they have reviewed might be more appropriate for setting a standard. You may hear some complaints so I thought I would forewarn you of that possibility.

It's nearing the end of the day and I will just have time to get this off to Federal Express.

Thanks for the opportunity to review this document.

Yours truly,

Herbert Cornish, Diplomate American Board of Toxicology

Recommendation for an Enforcement Standard and a Preventive Action Limit for Ammonia in Groundwater

(Draft)

Review

Herbert H. Cornish

June 25,1999

I will begin this review by briefly attempting to comment on the proposed questions, then I would like to make some additional comments.

1. Relevant Toxicity Data

The document presents only a limited review of the information on the toxicity of the ammonium ion. Admittedly there is little basic information available on the toxic response to ammonia. These data are complicated by the fact that ammonia is a natural component of animal metabolism. Thus dose levels and the mode in which ammonia is presented to man or animals affects the biological response. Free ammonia also reacts with water to produce ammonium hydroxide and rapidly reacts with other chemicals that may occur in natural water from various sources. This complexity makes risk assessment difficult and ammonium salts are often utilized in oral studies. There is some concern in the literature on the appropriate salt to be used in such studies since the anion may also affect the results. For example EPA has not accepted animal data utilizing ammonium chloride as a valid study of ammonia toxicity since the chloride ion may produce a metabolic acidosis . It can be argued that as a natural metabolite in animals there are mechanisms to handle readily the effects of both the ammonium and chloride ion and this is apparently true at low dose levels.

2. All Pertinent Data Reviewed

Most of the pertinent animal studies are reviewed and available human data is also presented. Considerable data concerning ammonia which may be relevant to risk assessment are not considered in the document. This includes information on mechanisms of ammonia and chloride toxicity since it is proposed that the use of ammonium chloride in human medicine be used as the basis for risk assessment. There is considerable information in pharmacology and toxicology texts and other relevant information in previous risk assessment documents that would be useful in interpretation of animal and human data on ammonia and its salts.

3. Need For Standard

It is indicated in the present document that new information is available which suggests that the EPA water quality standard might be reviewed. Admittedly the EPA standard is based on taste and odor as an indicator of possible toxic response. This does not appear to be a valid basis for developing safe exposure levels and it appears to have been used because no other good data were available. On the basis of known metabolic sources of ammonia I assume it was concluded that relatively low levels of ingestion could be tolerated. The need for better data is apparent. It is also true, unfortunately, that the proposed use of data based solely on an old traditional use of ammonium chloride as a diuretic and urine acidifying agent has not been documented as a safe level of exposure. No data are presented which would indicate that the medicinal dose was a reasonable LOEL or NOEL. There is only an indication that it has been used medicinally. No short or long term studies in humans or animals are presented to support the conclusion that the human dose is a reasonable LOEL. Admittedly, it may be as good as or better than some of the animal data available. Its use, however is questionable unless the need for a new standard has been documented.

4. Is Database Available

Whether or not there is sufficient appropriate data for calculation of a groundwater standard for ammonia has been the topic of considerable debate over many years. However, where good data are not available it may be necessary to use the best data to suggest an apparent safe

exposure level. This is what has happened with the ammonia level for water. In the absence of data EPA has suggested a level based on organoleptic data. No information has been provided in the present document to suggest whether this is a safe or unsafe level of exposure. Animal studies now reported in this document may provide the best available data for risk assessment .

5. Is the Proposed Standard Based on the Best Available Data.

This is a debatable point since there were no good data available that would be consistent with those normally used in risk assessment calculations. Because of the apparently low order of toxicity of ammonia and the ability of the body to handle ammonia in biochemical reactions EPA suggests the use of taste and odor as a basis for a standard. The present proposal makes use of a level of ammonium chloride utilized in medicine. This would seems a reasonable approach but it makes use of information on ammonium chloride rather than ammonia. Some reports suggest that this is not a suitable chemical to use since the anion may produce biological effects. In addition no data are presented to indicate the basis for the use of this compound in medicine. Certainly the available data are spare, however the present document reviews several recent animal studies that may be useful in risk assessment. See Discussion

6. Use of Uncertainty Factors

A factor of 10 is appropriate to correct for use of a LOEL in general risk assessment calculations.

The factor of 2 to convert from discontinuous exposure to continuous exposure is a judgmental figure and appears to be reasonable.

7. Protection Afforded by the Proposed Standard.

The proposed standard of 9.7 mg/L as ammonia N is obviously more likely to protect sensitive individuals (i.e. infants , those with chronic disease affecting liver or kidney function, those with debilitating illnesses such as cancer) than is the higher level of 34 mg/L of ammonia suggested by EPA. However, there are no data available to suggest that even the proposed lower level of exposure will protect such sensitive individuals. Neither of the proposed values are based on good animal or human studies.

8. Actions Supported by the Available Data.

Ammonia should be regulated with a health based standard derived from animal or human data obtained from good toxicological studies. Some studies are presented in the document which may be useful for risk assessment. By default, both EPA and the present document make use of minimal data in their proposed risk assessments for ammonia. It is not possible to determine which may be the most appropriate since both have serious deficiencies.

DISCUSSION

The discussion of which studies of ammonia are suitable for risk is almost a philosophical discussion rather than a scientific one.

The first question is whether or not there is a necessity for a new standard. The document suggests that "there is ample evidence that chronic exposure to ammonia in water can

contribute to the occurrence of disease and the exacerbation of existing illness in sensitive populations". Although several new studies are reported which appear to provide some suitable data they were evidently not considered suitable for risk assessment calculations. The document does state, however, that two of the studies were best suited for use in identifying a level at which to set an enforcement standard. However the final decision was made to base the standard on ammonia by using the data from a proposed dose schedule for ammonium chloride as a diuretic in children. Unfortunately this dose level was not supported by any data, animal or human, to validate that this is a safe level of exposure.

Often side effects of drugs are tolerated if the compound performs a useful function. As previously mentioned, EPA has suggested that data from studies with ammonium chloride not be used for risk assessment of ammonia because of the acidification provided by the chloride ion which may interfere with the response.

Thus we are faced with a dilemma. The EPA standard is based on taste and odor data while the proposed calculation is based on medicinal use of ammonium chloride in humans but no knowledge of whether it was either effective or safe at the proposed dose level.

On page six of the document it is stated that there is ample evidence that chronic exposure to ammonia in water can contribute to the occurrence of disease and the exacerbation of existing illness in sensitive populations. A review of these data (Kawano or Hata studies) suggest that they may be better suited for the calculation of an enforcement standard than either organoleptic data or undocumented medicinal use. Both of these studies use ammonia in water as the test solution. The Kawano study utilized a two or four week dosing schedule and reported reductions in mucosal thickness at two different dose levels. The Hata study examined the direct effect of ammonia in water on gastric mucosa and reported significant reduction of the fundic and pyloric glands of the gastric mucosa after 8 and 24 weeks of exposure. Both of these studies show effects at several dose levels. The Hata data are provided by a relatively long study which demonstrates a definite effect of ammonia in water after eight or twenty-four weeks of treatment.
These two studies in rats are uncomplicated by the use of an additional anion.

I would suggest that both of these studies be reviewed in detail and considered for possible use In development of an enforcement standard for ammonia.

PEER REVIEW COMMENTS
FROM

ARTHUR GREGORY

Peer Review
of
Draft Document Entitled
"Recommendation for an Enforcement Standard and a Preventive Action Limit for Ammonia in Groundwater"
(ERG Task No. 0023-192, under
State of Wisconsin Purchase Order No. NMT00001718)

Summary of Peer Review

The major problem with this document is the lack of distinction between the terms "ammonia" and "ammonium hydroxide". The introduction states, "Ammonia commonly reacts with water to form the ammonium ion (NH_4+), and environmental ammonia is usually found with these two forms in dynamic pH-dependent equilibrium." This is totally inadequate. The ATSDR document should be consulted for a better presentation of the equilibrium and the conditions under which it moves in one direction or the other. The dissociation constant (pKa of 9.3) is such that in the pH range of blood, the NH4+ ion constitutes about 99% of the total NH_4+ and NH_3 (Goodman and Gilman, 1990).

On Pages 3 and 4, there is a lack of consistency. On Page 3, background levels are given as 1-3 ppb. On Page 4, the background levels are given as 1-5 ppm, both using the same reference.

On Page 6, subchronic studies were described under the heading of "Chronic Studies."

Lastly, ammonia is both combustible and explosive (see ATSDR and "Encyclopedia of Occupational Health and Safety"). The second paragraph on Page 5 should be revised accordingly.

The Rettig study should be amplified. These data are important justifications for the need for a standard and indicate increased usage of ammonia.

On Page 4, the value for the mean blood ammonia concentration for adults of 70 micrograms per deciliter should not be given as if this were the only true mean value ever reported in the literature. The mean values reported vary with age, sex and analytical methodology. For example, the Geigy Scientific Tables (1984) report values that vary from 0.29 to 1.02 mg/L, depending on age, sex and analytical methodology.

I will now address each of the eight questions specifically asked regarding this draft document.

1. Does the background document present a good overview of the most recent relevant toxicity studies for ammonia in food or water?

This draft document presents a reasonable overview of the most recent relevant toxicity studies for ammonia in food and water. There is not a great deal of data available, but those studies reviewed present a valid picture of our present knowledge on ammonia.

2. Are you aware of toxicity information for ammonia that is relevant to this risk assessment that was not considered?

The studies utilized are the best that are presently available.

3. Does the toxicity information provided in the background document support the need for a health-based standard for ammonia in groundwater that is used to supply drinking water?

It is my opinion that it does. Although there are drawbacks in each of the studies, they support both the dose-response and the direct effects of ammonia in the risk determination paradigm.

I do feel that the use of the term "ammonia in groundwater" is a mistake. Nearly all the ammonia dissolved in groundwater is present as ammonium hydroxide. There is no way that the effects seen can be attributed to ammonia rather than ammonium hydroxide.

4. Is the existing toxicity database for ammonia sufficient to allow calculation of a groundwater standard that will ensure the safety of public and private drinking water supplies?

Ideally, while I would rather see a much sounder toxicity database utilizing larger animal groups and additional species, I consider the present database sufficient for calculations of a groundwater standard.

5. Is the proposed standard based on the most appropriate toxicity information available?

I am not aware of any data that is more extensive or more valuable than the data presented.

6. The proposed standard was established using a composite uncertainty factor of 20 based on the following considerations:

- a factor of 10 was used to account for the use of a lowest observed effect level (LOEL) rather than a no observed effect level (NOEL);
- A factor of 2 was used to account for the use of a recommendation for discontinuous exposure in developing a standard for continuous exposure to ammonia in water.

Are these uncertainty factors appropriate?

The terms should be LOAEL and NOAEL, not LOEL and NOEL, but the uncertainty factors used are similar to those used in most risk estimates. It is always a judgment call as to how we can be "safe enough" without extrapolating beyond reason. I consider the uncertainty factors appropriate. A factor of 10 should be used for extrapolation from experimental animals to humans if the animal studies are to be used.

On Page 10, no reference is provided for the value of 25 mg of ammonium chloride/Kg/day for children. Goodman and Gilman (1990) state only that ammonium chloride is available as an injection or tablets. On Page 695 they further state: "No effort is made herein to detail the specific therapy . . . ."

If the therapeutic guidance is to be used, an explicit reference should be provided to justify the use of 25 mg ammonium/Kg/day as an LOAEL. However, in my opinion the animal studies are more valid and should be used together with a factor of 10 to derive the standard.

7. Is the proposed standard (9.7 mg/L as N) likely to protect sensitive individuals (i.e., infants, those with chronic diseases affecting liver and kidney function, those with debilitating illnesses such as cancer) from toxicity due to ammonia-contaminated drinking water?

It is my opinion that the proposed standard will protect sensitive individuals if a factor of 10 is used in extrapolating from animals to humans and the animal studies are used to drive the standard. I do not consider the therapeutic guidance approach as valid. The reason for this is that the therapeutic guidance approach is based on the substance ammonium chloride, and *this* guidance is based on the acidic nature of the substance rather than the effect of the ammonium ion. On the other hand, the animal studies utilized ammonia dissolved in water and this risk is directly applicable to regulating the amount of ammonia that should be allowed to enter groundwater.

8. Which of the following actions is best supported by the toxicity studies presented?

- ✓ Ammonia should be regulated with a health-based standard derived from data such as those presented in the background document;
- ____ Ammonia should be regulated with a health-based standard derived from the taste/odor threshold;
- ____ Ammonia should be regulate so that the nitrogen burden from nitrate and ammonia not exceed the current standard for nitrate (10 mg/L nitrate-N + ammonia-N);
- ____ Ammonia should be regulated as a nuisance groundwater contaminant based on its taste/order threshold;
- ____ No regulation is needed for ammonia

The increased usage of ammonia direct injection into soils for fertilization should provide impetus for such regulation. This usage doubled in the last year alone (Riley, EPA). While such usage generally results in rapid conversion to nitrate, runoff from overloaded soils having low microbial counts could enter the groundwater. While such intrusion into municipal supplies would probably be diluted to a non-effect level, this may not be the case for groundwater supplying wells of individuals living in the country. Therefore, I consider the proposed regulation of value in protecting the health of the rural community.

PEER REVIEW COMMENTS
FROM

JAMES WITHEY

REVIEW OF DRAFT ' RECOMMENDATION FOR ENFORCEMENT STANDARD AND A PREVENTATIVE ACTION LIMIT FOR AMMONIA IN GROUNDWATER' APRIL 1999.

GENERAL COMMENTS.

I am a little unhappy about this document. After reviewing all of the published scientific literacture on the toxicology of ammonia and ammonium, No chronic studies using the oral or inhalation route were found.(All of those reviewed on pages 6, 7 and 8 are SUB-CHRONIC and should be placed in section 4.2).

The Enforcement Standard is based on information that appears to have no scientific basis! In fact there is no citation for the origin of ' 25mg/kg/day ' as the intermittent therapeutic dose. The Canadian Compendium of Pharmaceuticals and Specialties (1987) recommends ' 4 to 12g daily in divided doses every 4 to 6 hours ' which, for a 75kg man, works out at 160mg/kg/day. Although this is not the most recent copy of the Compendium, I have checked with the Canadian Health Protection Branch and the entry has not changed. I enclose a copy of the entry.

PAGE BY PAGE REVIEW.

Page 2, line 5. Give some indication of what is ment by ' high ' levels of ammonia in air.

Page 2, line 19. Again give some indication of what the concentration is in household ammonia. Page 5 has a statement that household ammonia contains 5 to 10% of ammonia.

Page 3, line 2. If the nitrification process yields nitrite and nitrate then the leached sediments may also contain nitrites well as nitrates.

Page 3, lines 2 to 4. I think you should explain the production of nitrogen in the absence of oxygen in a little more detail.

Page 3, line 20. What is ' photoelectric ' activity that forms hydroxyl radicals. Isn't the process photolysis?

Page 4, line 15. Note that sensitive sub-group populations are identified here. They are not considered in the development of the enforcement standard. EPA usually uses the uncertainty factor of x 10 for this parameter.

Page 5, line 3 and 4. This is not a dose. The volume and weight of the animals are needed to assess the dose. (More on ' dose ' later).

Page 5, line 9. The ' higher concentrations ' should be given in more informative terms.

Page 5, line 18. In Webster's report, were recoveries observed when one fluid ounce was ingested of 28% ammonia?

Page 6, Beginning line 11. Here, and in other studies cited later, the concentration of ammonia in the drinking water is given as a ' dose '. It is not. If the dose is not given in the publication, the US EPA uses an allometric relationship to obtain the water consumption per day, for a rat of a given weight, and calculates a dose per day. I enclose a reference and some photocopies of pages that allow these calculations from ' Recommendations for and Documentation of Biological Values for use in Risk Assessment' US. EPA/600/6-87/008, February, 1988.

For example, for a 200g rat the water consumption rate per day is calculated from the allometric relationship, given on page 1-11,

$$C = 0.1 \cdot W^{0.7337}.$$

which works out at 0.04 litres per day and, if the concentration of ammonia is 100mg/litre, comes out to 4mg/day and , if the rat weighs 0.2kg, the dose is 20mg/kg/day.

This procedure should be carried out for the Kawano et al. (1991), Hata et al. (1994), Toth, (1972), Tsujii et al. (1995) studies.

Page 6 . Section 4.3 Chronic Studies. There are no chronic studies in humans or animals. This statement should suffice for this section and all the discussion on pages 6, 7 and 8 should be transposed to section 4.2.

Page 7. Beginning on line 5. The Gupta et al. paper is listed in the reference section and its title is ' Toxicological studies of ammonium sulfate' (not sulfamate). I suspect this is an error in the reference list.

Page 7, line 7. I suppose that ' administered orally ' means ' by intubation '.If this is the case, say so.

Page 7. line 9. A 90 day study in rats is, classically, a sub-chronic study.

Page 7, line 19. The significant reductions in the ' height ' of the fundic and pyloric glands sounds odd. Shouldn't it be ' length '?

Page 7,last line. In the subsequent study by Hata et al. , for how long were the rats given water containing 200mg/litres?

Page 8, line 8. In the Deaton (1984) study, you should say what the route was (inhalation) and what the exposure regimen was.

Page 8, line 13. The study by Toth is the only study for which a chronic exposure was used. It is not clear whether only ammonia was used or whether all animals had been treated with the various hydrazine compounds as well. Please clarify. Also, were other observations than histological examination carried out?

Page 8 . Beginning line 21. In Tsujii's study, how large were the groups?

Page 9, lines 14 and 15. We have no chronic studies (except for a cancer study) available. Therefore this statement is erroneous and should be deleted.

Page 9, line 20. The literature contains data on the oral intake of ammonium compounds, not ammonia.

Page 10. It will be apparent from what has been stated in the General Comments, that I do not like the presentation in the first paragraph. I have pointed out, with referenced material (Canadian Compendium), that other figures for therapeutic doses of ammonium chloride have been recommended. I would like to see a reference as to where the 25mg ammonium/kg/day comes from. Secondly, this substance would not be given to patients suffering from kidney or liver disease i.e. it is not protective for ' special groups at risk' .

(This might be accommodated by using another uncertainty factor of x 10). Given that the therapy is dependent on the patient taking the high dose for only 3 to 4 days and then resting for ' a few days ' is this intermittent exposure accommodated by using an uncertainty factor of only 2 ?

Page 11, line 5. The US. EPA has used an organoleptic effect to set their Lifetime Health Advisory (taste). Was this because the published science was inadequate?

Page 12, line 7. The paper by Tsujii et al. (1995), in a sub-chronic study, certainly did show an interactive capacity for carcinogenesis and ammonia in promoting stomach cancer induced by MNNG.

SPECIFIC QUESTIONS ASKED BY EASTERN RESEARCH.

1.Quality of document. The document presents what little information there is on the toxicology of ammonia. None of these studies were, apparently, suitable for the derivation of an enforcement standard.

2. Are you aware of other toxicity data? No. I have enclosed the Canadian recommendations for therapeutic use of ammonia.

3. Does toxicity data support the need for a drinking water standard? No.Before this could be accomplished a well designed chronic study is desperately needed. Perhaps a human study could be constructed for this purpose.

4. Is toxicity data adequate to allow the development of a ground water standard that will ensure the safety for drinking water supplies?

Definitely not! I don't think we have sufficient data and, even with the application of larger uncertainty factors, we could not be sure that the number would be protective.

5. Is present standard based on the best information available?

For reasons that I have already expressed I think the scientific basis for the standard is extremely poor. If a more rational basis for the selection of the therapeutic dose

recommendations can be provided then we should have the best available information, but this would not beat a new, properly designed chronic study.

6. Appropriateness of the Uncertainty Factor. I don't think they are protective enough. I think that another uncertainty factor for sensitive sub-groups is necessary and we should think about one for the cancer promotion aspect. I am not sure, given the erratic dosage regimen suggested for the therapeutic application, that a factor of 2 is sufficiently protective either.

7. Is the present standard sufficient to protect sensitive groups at risk? Certainly not, for reasons that I have extensively covered in this review.

8. Which of the following actions is best supported by the toxicity studies presented?

...√... Ammonia should be regulated with a health- based standard (derived from data such as those presented in the background document) — doubtful.

.....Ammonia should be regulated with a health-based standard derived from the taste/odor threshold;

.....Ammonia should be regulated so that the nitrogen burden from nitrate and ammonia not exceed the current standard for nitrate (10mg/Lnitrate-N+ammonia-N);

.....Ammonia should be regulated as a nuisance groundwater contaminant based on its taste/odor threshold;

.....No regulation is needed for ammonia;

JAMES R. WITHEY, PhD.

June 19 1999.

ANNOTATED PAGES
FROM

JAMES WITHEY

DRAFT

Recommendation for an Enforcement Standard and a Preventive Action Limit for Ammonia in Groundwater

April, 1999

1.0 Introduction

Ammonia (NH_3) is a basic inorganic compound that occurs in the environment as a result of both natural and industrial processes. In nature, ammonia is a key constituent in the nitrogen cycle, the process by which nitrogen becomes available for use in the various biological activities for which it is required. Ammonia commonly reacts with water to form the ammonium ion (NH_4^+), and environmental ammonia is usually found with these two forms in dynamic pH-dependent equilibrium. Concentrated levels of ammonia from natural sources may result from accumulated animal wastes or from sewage treatment plants. Other natural sources include decaying vegetation and volcanic activity.

Commercially, ammonia is used widely as an agricultural fertilizer, as well as in refrigeration systems, household cleaners, and manufacturing processes. It is used in conjunction with chlorine to form chloramine, a common drinking water disinfectant. Concentrated levels of ammonia from commercial sources may commonly stem from the release of anhydrous ammonia to the environment or as effluent from industrial processes in which ammonia is used. The commercial synthesis of ammonia is considered to be a minor source, contributing no more than 5% of the total global ammonia budget.

2.0 Hazard Identification

2.1 Sources of Human Exposure

2.1.1 Inhalation

Ammonia may volatilize into the atmosphere from surface water. Most human exposures to elevated levels of ammonia result from inhalation of ammonia that has volatilized from household cleaning products. Inhalation of anhydrous ammonia may result in a serious, life-threatening inflammation of the respiratory tract, and may lead to the development of chronic bronchitis. Specific populations which may be exposed to high levels of ammonia in air include workers in industries involved in the manufacture or transport of ammonia-containing formulations, agricultural workers exposed to anhydrous ammonia or animal wastes, and people who live near agricultural sites where fertilizers are applied or livestock facilities which generate large amounts of animal waste.

2.1.2 Ingestion

Accidental or suicidal ingestion of household cleaning products may cause severe burns to the mouth, throat, esophagus and stomach. Ammonia evaporates quickly from surface water. In aerobic soil, nitrogen-fixing bacteria rapidly convert ammonia into nitrite (NO_2), which is converted into nitrate (NO_3) under aerobic conditions. Due to this metabolic activity and its volatility, ammonia is not found as a major contaminant of groundwater or surface water.

2.1.3 Dermal

Exposure may occur through dermal contact with household products containing ammonia. Exposure to anhydrous ammonia during the processing or application of fertilizers may result in severe burns to the eyes and skin.

2.2 Environmental Fate

2.2.1 Surface water and groundwater

Upon reaching surface waters, groundwater or sediment, ammonia may be transformed through two processes: nitrification and denitrification. Nitrification is an aerobic

process which yields the ionic compounds NO_2^- and NO_3^-. These may leach through sediment as nitrate or be taken up by aquatic plants. In the absence of oxygen, denitrification may transform ammonia into elemental nitrogen, a gas that is quickly lost to the atmosphere.

Ammonia can be acutely toxic to fish, and can cause symptoms such as loss of equilibrium, hyperexcitability, and increased breathing, cardiac output and oxygen uptake. High ammonia concentrations in water may result in convulsions, coma, and death. For freshwater fish, 48 and 96-hr LC_{50}s in the range of 0.024 to 4.60 mg/L have been reported. Reduced growth rate and pathological tissue changes have been reported at lower levels (WHO, 1986).

Background levels of ammonia in surface water and groundwater are rarely found to exceed 1 mg/L (ATSDR, 1990). Elevated ammonia levels may be found in surface waters near sewage treatment plants or large animal feedlots. In some cases, agricultural wastes may influence the levels of ammonia found in shallow wells. The rapid transformation of ammonia to nitrate is consistent with the observation of low levels of ammonia in groundwater.

2.2.2 Air

For ammonia that volatilizes into the atmosphere, a major transformation mechanism is a rapid reaction with acidic gases to form ammonium particulate. Ammonia may also react with hydroxyl radicals formed as a result of photoelectric activity. The resulting ammonium particulate may return to the earth's surface through wet or dry deposition.

Background worldwide atmospheric levels of ammonia are estimated at 1-3 parts per billion (ATSDR, 1990). Higher levels may be observed in locations near significant sources of ammonia, such as large animal feedlots.

2.2.3 Soil

Ammonia may reach soil through deposition or from the application of fertilizers. Ammonia in the soil is rapidly converted to nitrate or gaseous nitrogen, or may be taken up by plants. Background levels have been estimated at 1-5 parts per million, but are appreciably higher in soils on which fertilizers have been applied (ATSDR, 1990).

3.0 Absorption, Metabolism, Distribution and Excretion

In addition to the contribution from environmental sources, ammonia is produced in the human body as a result of the breakdown of protein, amino acids and other nitrogen-containing compounds by digestive tract bacteria. Ammonia that enters the gastrointestinal tract is rapidly absorbed. The mean blood ammonia concentration for adults is 70 micrograms/deciliter (Diaz, 1995). Absorbed ammonia is transported to the liver where it is converted to two metabolites: glutamine and urea. Glutamine is distributed to the tissues for use as a source of nitrogen for the synthesis of proteins, while urea is excreted by the kidneys. Persons suffering from diseases of the liver or kidneys may metabolize or excrete ammonia inefficiently, and are considered to constitute a sensitive subpopulation with respect to the toxic effects of ammonia. In patients with acute liver failure, ammonia may accumulate in the blood, brain and cerebrospinal fluid causing a condition termed hepatic encephalopathy. Other sensitive subpopulations include persons with genetic defects in ornithine transcarbamylase or the enzymes of the urea cycle, persons suffering from gout, and women in the last trimester of pregnancy who are at risk for toxemia of pregnancy (Dabney, 1996).

4.0 Dose-Response Assessments

4.1 Acute Toxicity

In experiments designed to demonstrate the acute toxicity of ammonia, glycols and other related compounds, Smyth and colleagues (1941) administered ammonium hydroxide in water to albino rats. Administration was by stomach tube in a single dose at concentrations as high as 1%, with 10 animals used per dosage. Animal deaths occurring within two weeks of dose administration were included in the assessment of lethality. An acute LD_{50} was reported at 350 mg/kg.

This is Not a dose

Household ammonia solutions typically contain 5-10% ammonia in water. These concentrations rarely cause burns, but can irritate the eyes, nose, throat, and upper respiratory tract. Higher concentrations such as? used in agricultural and industrial settings can cause irritation and severe burns of the eyes, lungs, upper airway, and skin. When heated to decomposition, ammonia emits toxic fumes of ammonia and nitrogen oxides. A study of emergency room records from 18 central Nebraska hospitals identified ammonia as the agricultural chemical most frequently associated with emergency room treatment or hospitalization (Rettig, 1987).

Suicidal or accidental ingestion of household ammonia can cause esophageal burns with late resulting strictures. Gastric, duodenal and jejunal lesions have also been reported. One teaspoonful of strong (28%) ammonia has been reported to be fatal but recoveries have followed ingestion of as much as one fluid ounce of this concentration? on several occasions (Webster, 1930).

Ingestion of milk contaminated with ammonia from a commercial refrigeration system resulted in acute illness among a group of Wisconsin school children in 1985. Reported symptoms included nausea and burning of the mouth and throat, and were observed within an hour after consuming contaminated milk. Analysis of milk from unopened cartons delivered to the school showed ammonia concentrations ranging from 530 to 1524 mg/L (CDC, 1986).

4.2 Subchronic Toxicity

Ammonium chloride has been used as a diuretic and urine-acidifying agent. Therapeutic dosage levels for adults range from 4 to 12 grams/day. Based on an average body weight of 70 kg, these are equivalent to 19 to 57 mg/kg/day as ammonium. The usual acidifying dose for children if 75 mg/kg/day (25 mg/kg/day as ammonium). The drug is given in four divided doses for three to four days, followed by a two-day rest period. If given continuously, particularly to patients with renal impairment, it may cause severe metabolic acidosis. Any use is contraindicated in patients with liver or renal disease since accumulation of ammonia in such patients may lead to central nervous system toxicity. Other adverse effects associated with the administration of ammonium chloride include gastric irritation, anorexia and electrolyte disturbances (ASHP, 1988).

Kawano and colleagues (1991) investigated the relationship between ingestion of ammonia in water and chronic atrophic gastritis in rats. In this study, groups of rats were given water containing 0.01% ammonia (100 mg/L) or 0.1 % ammonia (1000 mg/L) for either two or four weeks. A separate group of rats was retained as a control. Following exposure, the rats were sacrificed and their stomachs subjected to histological examination. Rats exposed to 0.01% ammonia exhibited significant reduction in the thickness of the antral mucosa in comparison with control rats following four weeks of exposure. Rats exposed to 0.1% ammonia showed significant reductions in mucosal thickness after two and four weeks of exposure, with reductions greater than those seen in the 0.01% exposure group. The authors concluded that ammonia produced by the gastric bacterium *Helicobacter pylori* likely plays a role in the development of chronic atrophic gastritis.

4.3 Chronic Studies

The chronic toxicity of ingested ammonia has not been studied in humans. Several subchronic animal studies have been conducted using drinking water or dietary exposure to ammonium hydroxide, ammonium chloride, and ammonium sulfamate. Systemic effects that have been observed include enlarged adrenal glands, alterations in blood pressure, and decreased body weight associated with decreased food intake.

Fazekas (1939) conducted a study on the effects of exposure to ammonium hydroxide (NH_4OH) on rabbits. Animals were given 100 mg NH_4OH/kg body weight on alternate days, then on a daily basis for 17 months. Test animals were found to have enlarged adrenal glands and elevated blood pressure.

a 90 day study in rat is not chronic

Gupta and colleagues (1979) conducted an investigation of the chronic toxicity of ammonium sulfamate in adult and weanling albino rats. Ammonium sulfamate was administered orally to groups of 20 rats in dosages of 100, 250 and 500 mg/kg/day, respectively, with another group of rats serving as controls. Doses were administered six days a week for 90 days. Significant decreases in group mean body weight were observed for the 500 mg/kg/day dose group of adult females weighed after 60 days and 90 days. A significant decrease in food consumption was observed in the 500 mg/kg/day dose groups of male and female weanlings after 90 days. No adverse effects relating to animal appearance, behavior or survival or organ histology were observed.

? intubation?

? refs say sulfate!

Hata and colleagues (1994) conducted an investigation of the effects of ammonia on gastric mucosa. Groups of 60 male Donryu rats were given drinking water with ammonia concentrations of 200 mg/L and 1000 mg/L, respectively, for 24 weeks, with a third group retained as a control. At eight intervals during the experiment, subgroups of six animals were extracted, sacrificed, and examined for histological changes in the gastric mucosa. Significant reductions in the height of the fundic and pyloric glands were observed in both treatment groups in animals sacrificed after eight and 24 weeks. The authors concluded that these findings are indicative of the direct toxicity of ammonia on the gastric mucosa.

Similar comment for Kawano et al

not chronic

In a subsequent experiment, the same researchers examined the effect of ammonia on the healing of gastric ulcers induced by treatment with acetic acid. Forty six-week-old male Donryu rats were infused with acetic acid by laparotomy to induce gastric ulcer formation. The animals were then divided into two groups: one given water containing 200 mg/L ammonia and one given untreated water. The induction of ulcers by treatment

convert to mg/kg/day

for how long?

with acetic acid was confirmed in all animals. Animals were sacrificed after four and eight weeks and their stomachs examined. Rats fed ammonia in water had ulcers significantly larger than controls after four and eight weeks of treatment, a finding the authors attributed to an impaired ability to repair gastric ulcers in the treatment group.

Not chronic.

4.4 Reproductive and Developmental Effects

Few data exist on the reproductive or developmental effects of ammonia exposure in humans or mammals. Decreased egg production has been demonstrated in birds and pullets exposed to ammonia (Deaton, 1984). An elevated ammonia tissue concentration in cows has been found to decrease conception rates and increase the calving-to-conception intervals (Visek, 1984). No data were located regarding the teratogenic potential of ammonia.

(inhalation) & how exposed how long

how? by the inhalation route

any info on how exposed and for how long

4.5 Carcinogenicity and Mutagenicity

a chronic study!!

Toth (1972) examined the carcinogenicity of ammonia in lifetime studies in mice. Ammonium hydroxide was administered under two sets of conditions: to five-week-old Swiss mice in drinking water at concentrations of 0.1% (1000 mg/L), 0.2% (2000 mg/L) and 0.3% (3000 mg/L); and to seven-week-old C3H mice in drinking water at 0.1% (1000 mg/L). All animals were either allowed to die or euthanized with ether when found in poor condition, and subjected to histological analysis. The incidence of tumors in the treated animals was similar to the incidence in control mice. The authors concluded that ammonium hydroxide does not exert a carcinogenic effect in mice.

convert to mg/kg/day

Tsujii and colleagues (1995) conducted an investigation of the relationship between exposure to ammonia in water and gastric carcinogenesis initiated by treatment with N-methyl-n'-nitrosoguanidine (MNNG). Groups of male Sprague-Dawley rats were given MNNG in drinking water for 24 weeks, after which groups were given either water containing 0.01% ammonia (100 mg/L) or tap water for another 24 weeks. Animals were sacrificed and their stomachs subjected to histological analysis. Rats fed ammonia in the

how many? per group

mg/kg/day please.

second phase of the experiment had a significantly higher incidence of stomach cancer, had a greater number of stomach tumors, and had tumors that were greater in size than control rats. The authors concluded that ammonia may play a role in the etiology of stomach cancer associated with *Helicobacter pylori*.

There are few data in the literature on the mutagenicity of ammonia. A number of researchers have reported that some evidence of mutagenicity in bacterial cells treated with lethal doses of ammonia. Because of the lethality of the administered dose, however, such findings have generally been interpreted as not indicative of any mutagenic effect (ATSDR, 1990).

4.6 Summary and Rationale

The goal of reviewing the toxicological data described above is to identify those data that provide appropriate guidance for recommending an enforcement standard and preventive action limit for ammonia in groundwater. While the number of studies investigating adverse outcomes relating to oral exposure to ammonia is small, the available data provide ample evidence that chronic exposure to ammonia in water can contribute to the occurrence of disease and the exacerbation of existing illness in sensitive populations. In accordance with the provisions of Chapter 160 Stats., it is therefore appropriate for the Department of Health and Family Services to issue a recommendation for an enforcement standard and a preventive action limit for ammonia in groundwater.

The literature includes a number of animal studies relating oral ammonia intake to a variety of health effects. In three of these studies (Kawano, 1991; Gupta, 1979; Tsujii, 1995), adverse health effects were observed following consumption of water containing ammonia or ammonium sulfamate at concentrations of 100 mg/L. Of these three, the studies by Kawano *et al* and Tsujii *et al* are best suited for use in identifying a level at which to set an enforcement standard. Given that the test animals in the study by Gupta *et al* were exposed to ammonium sulfamate, the lack of definitive information on the

toxicity of sulfamate may make it difficult to attribute the health effects observed in this study solely to exposure to the ammonium cation.

Data on the effects of subchronic or chronic human exposure to ammonia are extremely limited. Information on the use of ammonium chloride as a diuretic agent, however, provides important guidance in identifying an enforcement standard. It is recommended that therapeutic dosages of ammonium chloride not exceed 25 mg ammonium/kg/day for children, and that continuous use at that dose may cause systemic toxicity in patients with liver or kidney disease. As an oral dose considered potentially toxic upon continuous exposure, the maximum therapeutic dose of 25 mg ammonium/mg/day constitutes a lowest-observed adverse-effect level (LOAEL) for ammonia. Given that this recommendation directly relates to chronic human oral exposure to ammonia, this recommendation provides a more direct basis for recommending an enforcement standard than is offered by the studies by Kawano *et al* and Tsujii *et al*. For this reason, the recommendation on the therapeutic use of ammonium chloride is used in deriving the recommended enforcement standard and preventive action limit.

5.0 Recommendation of an Enforcement Standard and a Preventive Action Limit

In Wisconsin, the process by which groundwater enforcement standards and preventive action limits are to be set is specified in Chapter 160 of the Wisconsin Administrative Code. According to Chapter 160 Stats., the Department of Health and Family Services is charged with developing recommendations for enforcement standards on the basis of federal regulations and guidelines, such as the EPA's Maximum Contaminant Levels or Lifetime Health Advisories. The Department may recommend an enforcement standard that differs from a federal recommendation or standard "if there is significant technical information which is scientifically valid and which was not considered when the federal number was established".

The U.S. Environmental Protection Agency (EPA) has not established a health-based drinking water standard for ammonia. The EPA has issued a Lifetime Health Advisory for ammonia at 34 mg/L, which corresponds to the taste threshold for ammonia in water. Based on our review of current literature on the toxicity of ammonia, the Department of Health and Family Services finds that the federal lifetime health advisory may not adequately protect sensitive subpopulations, such as persons suffering from kidney or liver disease, against the toxicity of ingested ammonia.

will the 25mg/kg/day?

Therefore, in accordance with the provisions of Chapter 160 Stats., the Department of Health and Family Services recommends that a health-based groundwater enforcement standard be based on the human toxicity of ammonium chloride which has been used as a therapeutic agent. Following ingestion, ammonium chloride dissociates to produce the chloride anion and the ammonium cation. The chloride anion exerts a diuretic effect, but has little overt toxicity. In Wisconsin, chloride is currently regulated in public drinking water supplies and in groundwater as an indicator parameter. The literature suggests that the gastric irritation and neurotoxicity that have been associated with ingestion of ammonium chloride may be attributed to the local and systemic toxicity of ammonia.

To develop a health-based groundwater standard that will be protective against the toxicity of ingested ammonia, application of an uncertainty factor of 20 to the therapeutic dosage level is recommended. This includes a factor of 10 to convert from a human LOAEL to a NOAEL, and an additional factor of 2 to account for the use of information from a discontinuous, subchronic exposure. In accordance with Chapter 160 Stats., this recommendation is based on a daily intake of 1 L of water for a 10-kg child for whom drinking water constitutes the only source of ammonia exposure.

We consider of special groups at risk. factor of 2 is not rationale

$$\frac{25 \text{ mg/kg/day} \times 10 \text{ kg}}{20 \times 1 \text{ L/day}} = 12.5 \text{ mg/L as ammonium (9.7 mg/L as ammonia-nitrogen)}$$

In addition to the setting of an enforcement standard, Chapter 160 Stats. calls for the assignment of a preventive action limit. This limit is used as a tool in identifying

potential threats to groundwater and determining when additional monitoring may be appropriate. According to Chapter 160 Stats., the preventive action limit is to be set at 20% of the enforcement standard. For substances with carcinogenic, mutagenic or teratogenic properties or interactive effects, the preventive action limit is to set at 10% of the enforcement standard. In considering the data presented here, the Department of Health and Family Services finds that ammonia has not been shown to have carcinogenic, mutagenic or teratogenic properties or interactive effects. Therefore, a 20% preventive action limit is appropriate.

one study did show this! Tsuji (1995)

Recommended preventive action limit: 1.9 mg/L as ammonia-nitrogen

6.0 References

Agency for Toxic Substances and Disease Registry (ATSDR). 1990. Toxicological profile for ammonia. Address needed.

American Society of Hospital Pharmacists (ASHP). 1988. American Hospital Formulary Service - Drug Information 88. ASHP, Bethesda, MD.

Centers for Disease Control. 1986. Ammonia contamination in a milk-processing plant - Wisconsin. Morb Mortal Weekly Rep 35:274-275.

Dabney BJ, ed. 1996. Ammonia (REPROTEXT ® Document). In: REPROTEXT ® Database, Micromedex, Inc., Englewood, CO (Edition expiring October 31, 1996). ?

Deaton JW, Reece FN and Lott BD. 1984. Effect of atmospheric ammonia on pullets at point of lay. Poult Sci 63:384-385.

Diaz J, Tornel PL and Martinez P. 1995. Reference intervals for blood ammonia in healthy subjects, determined by microdiffusion. Clin Chem 41:1048.

Fazekas IG. 1939. Experimental suprarenal hypertrophy induced by ammonium hydroxide. Endokrinologie 21:315-337.

Gupta BN, Khanna RN and Datta KK. 1979. Toxicological studies of ammonium sulfate in rat after repeated oral administration. Toxicol 13:45-49.

Hata M, Yamazaki Y, Ueda T, Kato T, Kohli Y and Fujiki N. 1994. Influence of ammonia solution on gastric mucosa and acetic acid induced ulcer in rats. Eur J Histochem 38:41-52.

Kawano S, Tsujii M, Fusamoto H, Sato N and Kamada T. 1991. Chronic effect of intragastric ammonia on gastric mucosal structures in rats. Digest Dis Sci 36:33-38.

Rettig BA, Klein DK and Sniezek JE. 1987. Incidence of hospitalization and emergency room visits resulting from exposure to chemicals used in agriculture. Nebr Med J 72:215-219.

Smyth HF, Seaton J and Fischer L. 1941. The single dose toxicity of some glycols and derivatives. J Ind Hyg Toxicol 23:259-268.

Toth B. 1972. Hydrazine, methylhydrazine and methylhydrazine sulfate carcinogenesis in Swiss mice. Failure of ammonium hydroxide to interfere in the development of tumors. Int J Cancer 9:109-118.

Tsujii M, Kawano S, Tsuji S, Takei Y, Tamura K, Fusamoto H et al. 1995. Mechanism for ammonia-induced promotion of gastric carcinogenesis in rats. Carcinogenesis 16:563-566.

Visek WJ. 1984. Ammonia: its effects on biological systems, metabolic hormones, and reproduction. J Dairy Sci 67:481-498.

is this correct? or is it ~~sulfa~~ sulfamate

Webster RW. 1930. Legal medicine and toxicology. W.B. Saunders, Philadelphia.

World Health Organization (WHO). 1986. Environmental Health Criteria 54. WHO, Geneva.

ADDITIONAL REFERENCES
FROM

JAMES WITHEY

COMPENDIUM OF PHARMACEUTICALS AND SPECIALTIES 1987

THE CANADIAN REFERENCE
FOR HEALTH PROFESSIONALS

administration with MAO inhibitors has been considered an absolute contraindication; however, patients with refractory depression have received combination therapy without significant adverse effects. If used in combination therapy, give the drugs orally, avoid large doses and monitor the patient closely. Not recommended during the acute recovery phase following myocardial infarction, and in the presence of acute congestive heart failure.

Precautions: May block the antihypertensive action of guanethidine or similarly acting compounds.

Should be used with caution in patients with a history of seizures or urinary retention, or with narrow angle glaucoma or increased intraocular pressure.

Arrhythmias, sinus tachycardia, and prolongation of the conduction time have been reported, particularly with high doses. A few instances of unexpected death have been reported in patients with cardiovascular disorders. Myocardial infarction and stroke have also been reported with drugs of this class. Therefore, these drugs should be used with caution in patients with a history of cardiovascular diseases such as myocardial infarction and congestive heart failure.

Close supervision is required for hyperthyroid patients or those receiving thyroid medication.

Occupational hazards: May impair mental and/or physical abilities required for performance of hazardous tasks, such as operating machinery or driving a motor vehicle.

Pregnancy and lactation: Safe use during pregnancy and lactation has not been established. In pregnant patients, nursing mothers, or women who may become pregnant, weigh possible benefits against possible hazards to mother and child. Amitriptyline and nortriptyline are excreted in low concentrations in breast milk.

Schizophrenic patients and those with paranoid symptomatology may have increased symptoms; manic depressives may experience a shift to the manic phase. In these circumstances amitriptyline dosage may be reduced or a phenothiazine antipsychotic agent may be administered concurrently.

When given with anticholinergic agents or sympathomimetic drugs, close supervision and careful adjustment of dosages are required. May enhance the response to alcohol and the effects of barbiturates and other CNS depressants.

The possibility of suicide in depressed patients remains during treatment and until significant remission occurs; this type of patient should not have easy access to large quantities of the drug.

Concurrent electroshock therapy may increase the hazards of therapy; such treatment should be limited to patients for whom it is essential.

Discontinue the drug several days before elective surgery if possible.

Adverse Effects: Note: Included in this listing are a few adverse reactions not reported with this specific drug. However, pharmacological similarities among the tricyclic antidepressant drugs require that each reaction be considered when amitriptyline is administered.

Behavioral: activation of latent schizophrenia; high doses may cause temporary confusion or disturbed concentration, or rarely, transient visual hallucinations; hypomanic reactions; drowsiness which usually disappears with continuance of therapy; insomnia, giddiness, restlessness, agitation, fatigue, nightmares, disorientation, delusions, excitement, anxiety, and jitteriness.

Neurological: epileptiform seizures; numbness, tingling, paresthesias of the limbs, including peripheral neuropathy; dizziness, fine tremor, headache, ataxia, seizures, alteration in EEG patterns, extrapyramidal symptoms, tinnitus and incoordination; severe tremor only observed with high doses.

Autonomic: evidence of anticholinergic activity, such as urinary retention, reversible dilatation of the urinary tract, constipation, and more rarely, paralytic ileus of particular concern in the elderly; dry mouth, blurred vision and disturbance of accommodation.

Cardiovascular: a quinidine like effect and other reversible ECG changes such as flattening or inversion of T waves, and bundle branch block; orthostatic hypotension, hypertension, palpitation, arrhythmias, heart block, and, with toxic doses, ventricular tachycardia and fibrillation; myocardial infarction and stroke. A few instances of unexpected death have been reported in patients with cardiovascular disorders.

Toxic and allergic effects: bone marrow depression including agranulocytosis, eosinophilia, purpura and thrombocytopenia; jaundice rarely. Allergic type reactions manifested by skin rash, urticaria, photosensitization or swelling of the face and tongue and itching occurred rarely.

Gastrointestinal: nausea, epigastric distress, heartburn, vomiting, anorexia, stomatitis, peculiar taste, diarrhea, parotid swelling, black tongue.

Endocrine: testicular swelling and gynecomastia in the male, breast enlargement and galactorrhea in the female, increased or decreased libido, elevation and lowering of blood sugar levels.

Metabolic: increased appetite, weight gain or weight loss in some patients.

Ophthalmologic: precipitation of latent glaucoma or aggravation of existing glaucoma; blurred vision and mydriasis.

Miscellaneous: other side effects that may occur include fainting, weakness, urinary frequency, increased perspiration, and alopecia.

Withdrawal symptoms: abrupt cessation of treatment after prolonged administration may produce nausea, headache, and malaise; these are not indicative of addiction.

Overdose: Symptoms: High doses may cause temporary confusion, disturbed concentration, transient visual hallucinations, agitation, hyperactive reflexes, muscle rigidity, vomiting, or hyperpyrexia, in addition to anything listed under Adverse Effects. Based on amitriptyline's known pharmacologic actions, overdosage may cause drowsiness, hypothermia, tachycardia and other arrhythmic abnormalities such as bundle branch block, ECG evidence of impaired conduction and congestive heart failure. Other manifestations may be dilated pupils, convulsions, severe hypotension, stupor and coma. All patients suspected of having taken an overdose should be admitted to a hospital as soon as possible.

Treatment: Symptomatic and supportive. Empty the stomach as quickly as possible by emesis or gastric lavage. Follow with activated charcoal (50 to 100 g), plus saline cathartic every 4 to 6 hours during the first 24 hours after ingestion as the drug is enterohepatically recycled.

Monitor cardiac function for any signs of dysrhythmia. Asymptomatic patients should be monitored for 6 hours. Patients with ECG changes should be monitored for 24 to 48 hours after ECG has returned to normal.

Maintain ventilation; regulate body temperature.

Maintain fluid and electrolyte balance. Alkalinize blood to pH 7.4 to 7.5 with i.v. sodium bicarbonate. This may prevent tachycardia and other cardiac arrhythmias. Phenytoin may be used for arrhythmias refractory to sodium bicarbonate. Propranolol is effective but its negative inotropic effect may cause hypotension so it should be used with caution. Avoid quinidine and procainamide.

Diazepam i.v. may be given to control seizures.

Forced diuresis, peritoneal dialysis, hemodialysis or charcoal hemoperfusion are not effective in increasing elimination.

Since overdosage is often deliberate, patients may attempt suicide by other means during the recovery phase. Deaths by deliberate or accidental overdosage have occurred with this class of drugs.

Physostigmine has been useful in treatment of convulsions, cardiac arrhythmias and hallucinations. Not recommended for routine use or to reverse coma. Administer i.v. over 2 minutes to avoid seizures. Adult dose: 2 mg; pediatric dose: 0.5 mg. Repeat as required. Have atropine on hand to counteract excessive cholinergic effects.

Dosage: Orally: Dosage should be initiated at a low level and increased gradually, noting carefully the clinical response and any evidence of intolerance.

Initial dose for adults: 25 mg 3 times a day. If necessary, increase doses preferably in the late afternoon and/or bedtime to total of 150 mg a day.

Hospitalized patients may require 100 mg a day initially; increased gradually to 200 mg a day if necessary. A small number need as much as 300 mg a day.

Adolescent and elderly patients: In general, lower dosages recommended: 10 mg 3 times a day with 20 mg at bedtime may be satisfactory.

Maintenance dose is usually 25 mg 2 to 4 times a day. When satisfactory improvement has been reached, reduce to lowest amount that will maintain relief of symptoms.

Children: Not recommended for treatment of depression in children under 12 years of age.

Enuresis: 10 mg at bedtime for children under 6 years of age. In older children increase dosage as necessary, up to 25 mg at bedtime.

Parenterally: 20 to 30 mg i.m. 4 times a day. Change to oral route as soon as possible.

Reviewed 1986

AMMONIUM CHLORIDE

Ammonium Muriate

Diuretic—Urinary Acidifier

Pharmacology: Ammonium chloride is rapidly absorbed from the gastrointestinal tract. The ammonium cation is converted into urea in the liver. Chloride ion causes an increased chloride load on the renal tubules such that sodium and an iso-osmotic quantity of water are excreted with the excess chloride. A mild metabolic acidosis accompanies the mild diuresis. This has been used, in the past, to increase the diuretic effect of mercurial diuretics.

Indications: Ammonium chloride is used as a weak diuretic and in small doses as an ingredient of expectorant cough mixtures.

Ammonium chloride has been used in severe states of metabolic alkalosis.

Ammonium chloride has been used to acidify the urine in patients with amphetamine overdosage in order to hasten the urinary excretion of this drug.

Ammonium chloride has also been used for its diuretic effect in premenstrual edema and Ménière's disease.

Contraindications: Presence of advanced renal or hepatic disease.

Precautions: Use with caution in the management of cardiac edema.

Adverse Effects: Hyperchloremic metabolic acidosis, excessive doses or prolonged use may cause gastric upset, nausea or vomiting thirst, headache, hyperventilation, progressive drowsiness, mental confusion. Rapid i.v. injection may produce irregular breathing bradycardia and twitching.

Overdose: Treatment: For acidosis and electrolyte loss, i.v. sodium bicarbonate or sodium lactate. Correction of hypokalemia may be necessary.

Dosage: The dosage of ammonium chloride as a diuretic or urinary acidifier is 4 to 12 g daily in divided doses every 4 to 6 hours. The average dose is about 8 g. The drug is more effective as a diuretic when given for 3 to 4 days followed by a rest period of a few days after which therapy is again resumed.

As an expectorant, ammonium chloride is given in doses of 500 mg taken with a glassful of water every 2 to 4 hours.

Reviewed 1987

AMOBARBITAL ◇ AMOBARBITAL SODIUM ◇

Amylobarbitone ***Sedative—Hypnotic***

Indications: Oral amobarbital and amobarbital sodium preparations are indicated in conditions requiring degrees of sedation ranging from minimal doses for the relief of anxiety and tension to hypnotic doses for sleep and for preanesthetic medication.

Amobarbital sodium may be used i.v. or i.m., for the control of convulsive seizures such as may be due to chorea, eclampsia, meningitis, tetanus, procaine or cocaine reactions, or poisoning from such drugs as strychnine or picrotoxin. It also may be administered for the management of catatonic and negativistic reactions, manic reactions, and epileptiform seizures. It is also useful in narcoanalysis and narcotherapy and as a diagnostic aid in schizophrenia in experienced hands.

Contraindications: Patients with porphyria, severely impaired liver function, sleep apnea, suicidal potential and alcoholism. Do not use in the presence of uncontrolled pain as excitement may be produced. Do not administer to patients who are known to be hypersensitive to barbituric acid derivatives. Should not be administered to elderly patients who exhibit nocturnal confusion or restlessness from sedative hypnotic drugs. Persons who are known to be, or are likely to become, dependent on sedative hypnotic medications.

Precautions: May be habit forming. Use with caution in patients with decreased liver and renal function, since a prolongation of effect may occur.

Occupational hazards: Amobarbital may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a vehicle or operating machinery.

The concomitant use of alcohol or other CNS depressants may have an additive effect. Warn patients accordingly.

Drugs interactions: Barbiturates induce liver microsomal enzyme activity and may thus decrease blood concentrations and clinical efficacy of drugs given concurrently. It is necessary to monitor closely the dosage of oral anticoagulants, theophylline and other drugs when initiating or discontinuing barbiturate therapy.

A reduced efficacy and increase in incidence of breakthrough bleeding have been reported in oral contraceptive users treated concomitantly with barbiturates.

Prolonged use of barbiturates, even in therapeutic dosages, may result in psychological dependence. Withdrawal symptoms may occur after chronic use of large doses, resulting in delirium, convulsions, or death.

Pregnancy and lactation: Barbiturates readily cross the placental barrier and drug traces have been found in the breast milk of nursing mothers. Therefore, use of this drug should be avoided during pregnancy and lactation.

Dosage and rate of administration should be selected with great care in patients with hypertension, hypotension, or pulmonary or cardiovascular diseases. Rarely, rickets and osteomalacia have been reported following prolonged usage of barbiturates.

Amobarbital sodium is not recommended as an anesthetic agent, but if a patient develops physical signs of severe depression, he should be treated as though deeply anesthetized. Pulmonary edema may complicate long periods of unconsciousness.

If the condition of the patient justifies the i.v. administration of amobarbital sodium, close hospital supervision is also indicated.

If rapidly induced, deep, or protracted hypnosis is not necessary, the effect of amobarbital sodium should be obtained with oral preparations.

Adverse Effects: Idiosyncrasy, in the form of excitement, hangover, or pain, may appear. Hypersensitivity reactions occur in some patients especially in those with asthma, urticaria, or angioneurotic edema.

Overdose: Symptoms: Respiratory depression, depression of superficial and deep reflexes, constriction of the pupils to a slight degree (though in severe poisoning they may dilate), decreased urine formation, lowered body temperature, and coma.

Treatment: General management should consist in symptomatic and supportive therapy, including gastric lavage, administration of i.v. fluids, and maintenance of blood pressure, body temperature, and adequate respiratory exchange. An artificial kidney will increase the rate of removal of barbiturates from the body fluids.

PB88-179874

EPA/600/6-87/008
February 1988

RECOMMENDATIONS FOR AND DOCUMENTATION OF BIOLOGICAL VALUES FOR USE IN RISK ASSESSMENT

EPA Project Officer
K. Blackburn

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
OFFICE OF HEALTH AND ENVIRONMENTAL ASSESSMENT
OFFICE OF RESEARCH AND DEVELOPMENT
U.S. ENVIRONMENTAL PROTECTION AGENCY
CINCINNATI, OH 45268

TABLE 1-2

Reference Body Weights (kg)

Group	Species/Strain	Sex	Weaning	Subchronic	Chronic	Mature
Primates	monkey, rhesus	M	1.0		10.9	12
		F	1.0		8.0	9
					(0-35 years)	(10-35 years)
	chimpanzee	M	3.8		19.25	20
					(0-55 years)	(adult)
Laboratory rodents	mice/BAf1	M	0.008	0.0223	0.0261	0.035
		F	0.007	0.0204	0.0222	0.030
						(1 year)
	mice/B6C3F1	M	0.009	0.0316	0.0373	0.040
		F	0.011	0.0246	0.0353	0.035
						(1 year)
	rats*/	M	0.031	0.180	0.380	0.40
	Fischer 344	F	0.030	0.124	0.229	0.25
						(1 year)
	rats/Long-Evans	M	0.040	0.248	0.472	0.50
		F	0.038	0.179	0.344	0.35
						(1 year)
	rats/	M	0.053	0.263	0.518	0.55
	Osborne-Mendel	F	0.052	0.201	0.389	0.40
						(1 year)