Hazard Classification Issues for Mixtures: Reaction Products

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"The times, they are a changin'…" - Bob Dylan

Outline

- Reaction products in the world of lubricant formulation
  - "Synthetic" steel metalworking machining fluid as an example
- Thinking like a chemist v. thinking like an SDS author
  - lab performance tests, r.m. availability, costs, field tests, Sec 3?
- Providing ferrous metal corrosion protection
- Reaction product registration rules (US, EU)
- How do I handle reaction product issue?
- HCS 2024
  - New Appendix A and trade secrets
  - Section (d)(1)(ii)
- What to do next and looking ahead

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Lubricant Formulations

- Engine oils
  - Passenger car motor oils, Heavy Duty engine oils
- Industrial Lubricants
  - Hydraulic oils, way lubes, gear oils
  - Metalworking fluids (MWF)
    - "Straight oil" formulations
    - Water-miscible formulations
      - "Soluble oil" formulations
      - "Semisynthetic" formulations
      - "Synthetic" formulations

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Thinking Like a Chemist

- What laboratory bench & field tests must I meet?
  - Minimal eye and skin irritation (minimize 1° amine)
  - Machinability (include inverse soluble nonionic)
  - Hard water stability (monobasic, $<C_8$; dibasic, $<C_{12}$)
  - Corrosion protection
    - Metal being machined (aluminum; steel; brass)
    - Steel machine tool surfaces (cast iron chip rust protection)
  - Stability against microbiological attack (biocide)
  - Raw material availability
  - Cost of formulation
  - Section 3 SDS ingredient list

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Thinking Like an SDS Author

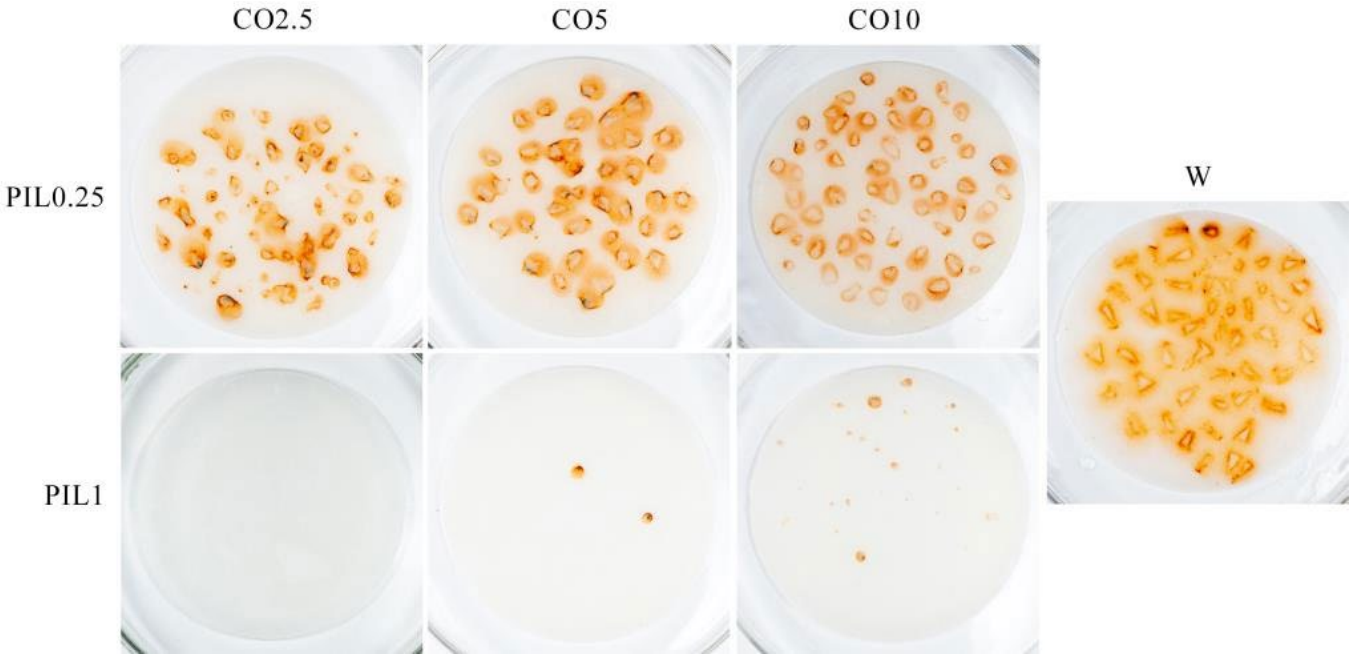
- "I've got a thousand SDS to maintain so here's what I need from my laboratory chemists…"
  - A formula I can input into Section 3 with:
    - CAS numbers which are registered for use in all the jurisdictions in which marketing/sales want to sell

    Please! Calculate reaction products: you're the chemist!
  - Physical property test results which match Section 9 headings
  - Your thoughts (and this is new) on any hazards arising from chemical reaction products from known or reasonably anticipated uses or applications?

"I am not clairvoyant or a mind reader!"

Thinking Like a Chemist

- Providing ferrous metal corrosion protection
  - Corrosion protection (cast iron chip test: ASTM D4627-22 or IP 287/08(2014))



Thinking Like a Chemist

- Cast iron chip corrosion protection
  - Turns out that combinations of an alkanolamine and an organic fatty acid add corrosion protection functionality to a synthetic MWF formulation
  - BUT, not all combinations work: best protection is provided by specific combinations of short straight or branched chain carboxylic acids (C_7-C_{10}) and/or a dibasic acids (C_6-C_{12}) and alkanolamines like TEA (triethanolamine, 3°) or primary amines (MEA, MIPA or amino-2-methyl-1-propanol, AMP)

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Reaction Product Registration Rules

- Chemical reactants must be on inventory
- What about chemical reaction products?
  - Depends on whether you have “intended” to create a reaction product or the reaction product is “incidental.”
- Let’s look at specific examples from EPA and from ECHA…

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EPA Reaction Product Registration Rules

- 40 CFR 720.30(h)(7) – Chemicals not subject to notification requirements
  - (h)(7) Any chemical substance which results from a chemical reaction that occurs when (i) a stabilizer, colorant, odorant, antioxidant, filler, solvent, carrier, surfactant, plasticizer, corrosion inhibitor, antifoamer or defoamer, dispersant, precipitation inhibitor, binder, emulsifier, deemulsifier, dewatering agent, agglomerating agent, adhesion promoter, flow modifier,

GHS RESOURCES

EPA Reaction Product Registration Rules

- 40 CFR 720.30(h)(7) – Chemicals not subject to notification requirements
  - (h)(7) (continued)… pH neutralizer, sequesterant, coagulant, flocculant, fire retardant, lubricant, chelating agent, or quality control reagent functions as intended, or (ii) a chemical substance, which is intended solely to impart a specific physiochemical characteristic, functions as intended.

EPA Reaction Product Registration Rules

- March 6, 2001 – letter of interpretation from Ms. Rebecca Cool

"As you noted, a 1994 letter from Joseph Carra, former Deputy Director, OPPT, to Ms. Randall provides guidance…"

  - 2) "the substance does not provide the primary properties that determine the use of the product or mixture distributed in commerce even though it may impart certain physicochemical characteristics to the product or product mixture of which it is a part, and…"

EPA Reaction Product Registration Rules

- March 6, 2001 – letter of interpretation (cont.)
  - 3) “the substance is not itself the one intended for distribution in commerce. Although it may be a component of the product mixture or formulation actually distributed in commerce, it has no commercial purpose separate from the product mixture or formulation of which it is a component.”

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EPA Reaction Product Registration Rules

- March 6, 2001 – letter of interpretation (cont.)

  "You specifically asked about fatty acid-alkanol amine salts, phosphate ester-alkanolamine salts, and boric acid alkanolamine salts. In each case, the salts have some desirable properties (supporting an emulsion, dispersibility, enhanced microbial resistance) but you state that [while] the components of the salts have specifically intended functions, the specific salts are not intentionally formed (or even known to be formed), and none is formed for distribution in commerce under its own identity."

GHS RESOURCES

EPA Reaction Product Registration Rules

- 1994 – letter of interpretation

The following two examples may be helpful in illustrating the application of the aforementioned criteria:

In the first example, an insoluble acid polymer is converted to its soluble amine salt during an ink formulation process in which other ingredients are added. The polymer salt formed as a result of a chemical reaction that brings the insoluble acid polymer into solution is an excluded substance. Although the polymer salt imparts certain physicochemical properties to the final commercial product, i.e., the ink, of which it is a part, it (1) does not itself contribute a primary property that is essential to the functioning of the ink as a viable commercial product, (2) is not itself the product intended for distribution

EPA Reaction Product Registration Rules

- 1994 – letter of interpretation

AUG 01 '94 12:26 ILMA

in commerce as a chemical substance *per se*, and (3) has no commercial purpose separate from the ink formulation. In this case, the ink formulator is interested in manufacturing an ink, not in producing the polymer salt itself. However, if a person manufactures the same polymer salt for distribution in commerce as a chemical substance *per se*, that salt then becomes a reportable substance.

EPA Reaction Product Registration Rules

- 1994 – letter of interpretation

In the second example, an antistatic agent used in a yarn treatment product is made by adding an amine in aqueous solution to a mixture of an acid precursor of the antistatic agent and other ingredients that are needed for the formulation. The salt formed as a result of the neutralization reaction provides the primary properties that are responsible for the product functioning as an antistatic agent. The salt in this case is a reportable substance, even though it remains in solution and is not separately isolated as a solid material.

In both of these cases, salts have been formed as a result of a pH neutralization reaction. If the resulting salt does not impart any properties that are responsible for the primary performance characteristics of the product, and is not manufactured for distribution in commerce as a chemical substance *per se*, it is not a reportable substance. However, as the second example illustrates, if the function of the neutralization reaction is to produce a salt that provides a primary property responsible for the use of the formulated product, the salt becomes a reportable substance.

GHS RESOURCES

ECHA Reaction Product Registration Rules

Guidance for Annex V

ECHA Reaction Product Registration Rules

Guidance for Annex V **Version 1.1 – November 2012**

ATTACHMENT 1: IONIC MIXTURES[23]

In order to provide a specific physicochemical characteristic, water is added to mixtures of ionic substances (salts, acids and bases). The ionic pairs in equilibrium in the aqueous solution are then the result of the water functioning as intended and would consequently not be considered to be themselves manufactured, imported or placed on the market and may under well defined conditions qualify for an exemption under entries 3, 4(a) or 4(b) of Annex V as explained hereafter.

In order for this exemption to be applicable, the following conditions must be fulfilled:

1. All starting substances (salts, acids and bases) of the aqueous solution must be registered;

2. None of the salts in the aqueous solution is isolated from the solution; and

3. The salts remain in their ionic form in the solution.

These three conditions equally apply to imported solutions. In particular, this requires that all starting substances of the imported solution must be known and registered in the EU; otherwise the exemption does not apply.

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ECHA Reaction Product Registration Rules

For solutions of salts in water no registration is required of ionic pairs as long as the combinations of ions co-exist with their different equilibria in the solution and no salts are isolated. In this context, it might be useful to clarify that

(1) whenever ionic pairs exist only as a part of the chemical equilibrium in the aqueous solution, they are not themselves considered to be manufactured, imported or placed on the market and thus do not require registration.

(2) whenever a salt is isolated from the solution, it is manufactured and needs to be registered.

(3) deliberate neutralisation of acids or bases to form the corresponding salts, including neutralisation during formulation, is usually a manufacturing process and is not covered by this exemption.

It should be noted that although the registration of substances ionised in water as described above is deemed inappropriate and is therefore exempted, the potential risks associated with the substances ionised in water must be taken into account in the chemical safety assessment of the starting materials (i.e. salts, acids or bases introduced in the aqueous solution), where applicable.

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How Do I Handle Reaction Product Issue?

- Did the chemist "intend" to create a specific combination of alkanolamine and organic acid?
  - If "intended" – or if isolated as a manufacturing intermediate, the reaction product should be on TSCA, DSL, ECHA, or other inventory where you intend to market your product.
  - If "unintended," use the 720.30(h)(7) exemption (EPA), Ionic Mixture exemption (ECHA) or similar exemption
- BUT, how do I construct the SDS ingredient list?

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“Synthetic” Steel MWF Formulation

Ingredient	CAS number	Wt %
Water	7732-18-5	59.000
Nitrilo-2,2',2"-triethanol (TEA, 99.5%)	102-71-6	16.000
2-aminoethanol (MEA)	141-43-6	3.000
3,5,5-trimethylhexanoic acid ("isonoanoic acid")	3302-10-1	5.000
commercial mixture of azelaic acid, dodecanedioic acid, undecanedioic acid	1852-04-6 (25-50%); 693-23-2 (25-50%); 123-99-9 (10-27%)	5.000
nitric acid, reaction products with cyclododecanol and cyclododecanone, by products from, high boiling fraction	72162-23-3	5.000
Oxirane, 2-methyl, polymer with oxirane	9003-11-6	6.000
Poly[oxyethylene(dimethyliminio(dimethyliminio)ethylene dichloride, 60%	31512-74-0	1.000
		100.000

SDS AUTHOR: “NOW WHAT DO I DO???”

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How Do I Handle Reaction Product Issue?

- Conversation with chemist: what, if anything, was an “intended” reaction product or is it already isolated as a manufacturing intermediate? (I contend that the specific combination of alkanolamine and fatty acids to give best rust protection could arguably be an “intended” reaction product?)
- Where will the product be marketed? Reaction products of interest need to be on that country/EU inventory. (And reported in IURs.)

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How Do I Handle Reaction Product Issue?

- Next: two (maybe three?) general approaches:
  - Can any of the alkanolamine-organic acid combinations be thought of as reaction products, even if not intended? (Another conversation with your chemist: what are the pKa's and pKb's of the ingredients? Stronger acids do react with stronger bases; weaker acids/weaker bases, not so much.)
  - Or, do I base the hazard classification on all of the included raw materials (even though I know they are neutralized)?
  - Can I take advantage of new Appendix A in HCS 2024 and use NAMs to test for the most common hazards, eye and skin irritation/corrosion?

“Synthetic” Steel MWF Formulation

Ingredient	CAS number	Wt %
Water	7732-18-5	59.000
Nitrilo-2,2',2"-triethanol (TEA, 99.5%)	102-71-6	3.710
2-aminoethanol (MEA)	141-43-6	0.421
isononanoic acid, compound with 2-aminoethanol	67801-50-7	6.929
nitric acid, reaction products with cyclododecanol and cyclododecanone, by products from, high boiling fraction, compounds with triethanolamine	1078712-94-3	11.939
azaleic acid, compound with 2-aminoethanol (1:2)	94108-49-3	1.649
undecanedioic acid, compound with nitrilo-2,2',2"-triethanol (1:2)	85030-07-5	4.760
dodecanedioic acid, compound with nitrilo-2,2',2"-triethanol (1:2)	85030-08-6	4.591
Oxirane, 2-methyl, polymer with oxirane	9003-11-6	6.000
Poly[oxyethylene(dimethyliminio(dimethyliminio)ethylene dichloride, 60%	31512-74-0	1.000
		100.000

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Chemical Salt Testing Results

Salt	CAS Number	Estimated Substance Classification, Eye (BCOP)	Estimated Substance Classification, Skin Irritation	Estimated Acute Toxicity Classification
TEA + dibasic acids	107871-94-3	Not classified, not an eye irritant	Uncategorized, not a dermal irritant	GHS Acute Tox 5 or unclassified (OSHA)
DGA + dibasic acids	292849-36-6	Not classified, not an eye irritant	GHS Cat 3 mild dermal irritant or unclassified (OSHA)	GHS Acute Tox 5 or unclassified (OSHA)
AMP + tall oil fatty acids	67701-21-7	Mild eye irritant, GHS Eye Cat 2B	GHS Category 1C skin corrosive	GHS Acute Tox 5 or unclassified (OSHA)
TEA + isononanoic acid	67801-51-8	Moderate eye irritant, GHS Eye Cat 2A	Uncategorized, not a dermal irritant	GHS Acute Tox 5 or unclassified (OSHA)
MEA + isononanoic acid	67801-50-7	Severe eye irritant, GHS Eye Cat 1	GHS Cat 3 mild dermal irritant or unclassified (OSHA)	GHS Acute Tox 5 or unclassified (OSHA)

HCS 2024?

- Can I take advantage of new HCS 2024 rules which further allow incorporation of *in vitro* test data?

	No/Insufficient data ↓		
3:	Existing *ex vivo/in vitro eye* data[d] ↓ ↘ No/Insufficient data/Negativeresponse ↓	Positive: serious eye damage Positive: eye irritant	**Category 1** **Category 2**[b]
4:	pH-based assessment (with consideration of acid/alkalinereserve of the chemical) [e] ↓ Not pH extreme, no pH data orextreme pH with data showing low/no acid/alkaline reserve ↓	pH ≤ 2 or ≥ 11.5 with high acid/alkaline reserve or no data for acid/alkaline reserve	**Category 1**
5:	↗ Validated Structure Activity Relationship (SAR) methods ↓ No/Insufficient data ↘ ↓	Severe damage to eyes Eye irritant Skin corrosive	**Category 1** **Category 2**[b] **Category 1**
6:	Consideration of the totalweight of evidence [f] ↘	Serious eye damage Eye irritant	**Category 1** **Category 2**[b]
	No concern based on		

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HCS 2024

- Can I take advantage of new HCS 2024 rules which further allow incorporation of *in vitro* test data?

[c] Existing animal data should be carefully reviewed to determine if sufficient serious eye damage/eye irritation evidence is available through other, similar information. It is recognized that not all skin irritants are eye irritants. Expert judgment should be exercised prior to making such a determination;

[d] Evidence from studies using validated protocols with isolated human/animal tissues or other non-tissue-based, validated protocols should be assessed. Examples of internationally accepted, validated test methods for identifying eye corrosives and severe irritants (i.e., Serious Eye Damage) include OECD Test Guidelines 437 (Bovine Corneal Opacity and Permeability (BCOP)), 438 (Isolated Chicken Eye (ICE) and 460 (Fluorescein leakage (FL)). Presently there are no validated and internationally accepted in vitro test methods for identifying eye irritation. A positive test result from a validated in vitro test on skin corrosion would lead to the conclusion to classify as causing serious eye damage;

[e] Measurement of pH alone may be adequate, but assessment of acid/alkaline reserve (buffering capacity) wouldbe preferable. Presently, there is no validated and internationally accepted method for assessing this parameter;

HCS 2024

- To remember: in Section 3, if you are claiming the exact formulation to be a trade secret, you need to use the prescribed concentration ranges, e.g.,

(A) From 0.1% to 1%;

(B) From 0.5% to 1.5%;

(C) From 1% to 5%;

(D) From 3% to 7%;

(E) From 5% to 10%;

(F) From 7% to 13%;

(G) From 10% to 30%;

(H) From 15% to 40%;

(I) From 30% to 60%;

(J) From 45% to 70%;

(K) From 60% to 80%;

(L) From 65% to 85%; and

(M) From 80% to 100%.

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Known or Reasonably Known Hazards

The challenge of the newly added/interpretation of HCS 2024

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HCS 2024

- 1910.1200(d)(1)(ii)

…The hazard classification shall include any hazards associated with the chemical's intrinsic properties including:

(i) A change in the chemical's physical form; and

(ii) Chemical reaction products associated with known or reasonably anticipated uses or applications.

Federal Register :: Hazard Communication Standard (correction, October 9, 2024)

HCS 2024

- 1910.1200(d)(1)(ii)
- What might go wrong with a MWF if it is mis-managed in the field?
  - Dermatitis or skin irritation
    - If concentration is too high or MWF is “dirty”
  - Respiratory disease
    - If ventilation is poor and microbiology is poorly controlled

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HCS 2024

- 1910.1200(d)(1)(ii)
- What might a (d)(1)(ii) entry on a MWF SDS look like?

Conditions	Chemical hazard classification	Category	Signal Word	Hazard Statement
Poorly filtered metalworking fluids with excessive dermal exposure	Skin irritation or dermatitis	Category 2	Warning	Causes skin irritation or dermatitis

Looking Ahead

- What to do?
  - Train your chemists to think like you, an SDS Author!
  - Reach agreement on what are “intended” reaction products v. “incidental” reaction products.
  - Agree on what might be ”…chemical reaction products associated with known or reasonably anticipated uses or applications.”

Looking Ahead

- Looking ahead to the future (Or, is the future already here???)
  - How will artificial intelligence (AI) help in creating better SDSs, including correct classifications and Sec. 3 ingredient lists?
  - Have you incorporated documentation of the many steps needed to classify your products and write SDSs and labels in your ISO 9000 quality system (ISO 9001:2026 is coming soon!)

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Any Questions ?