

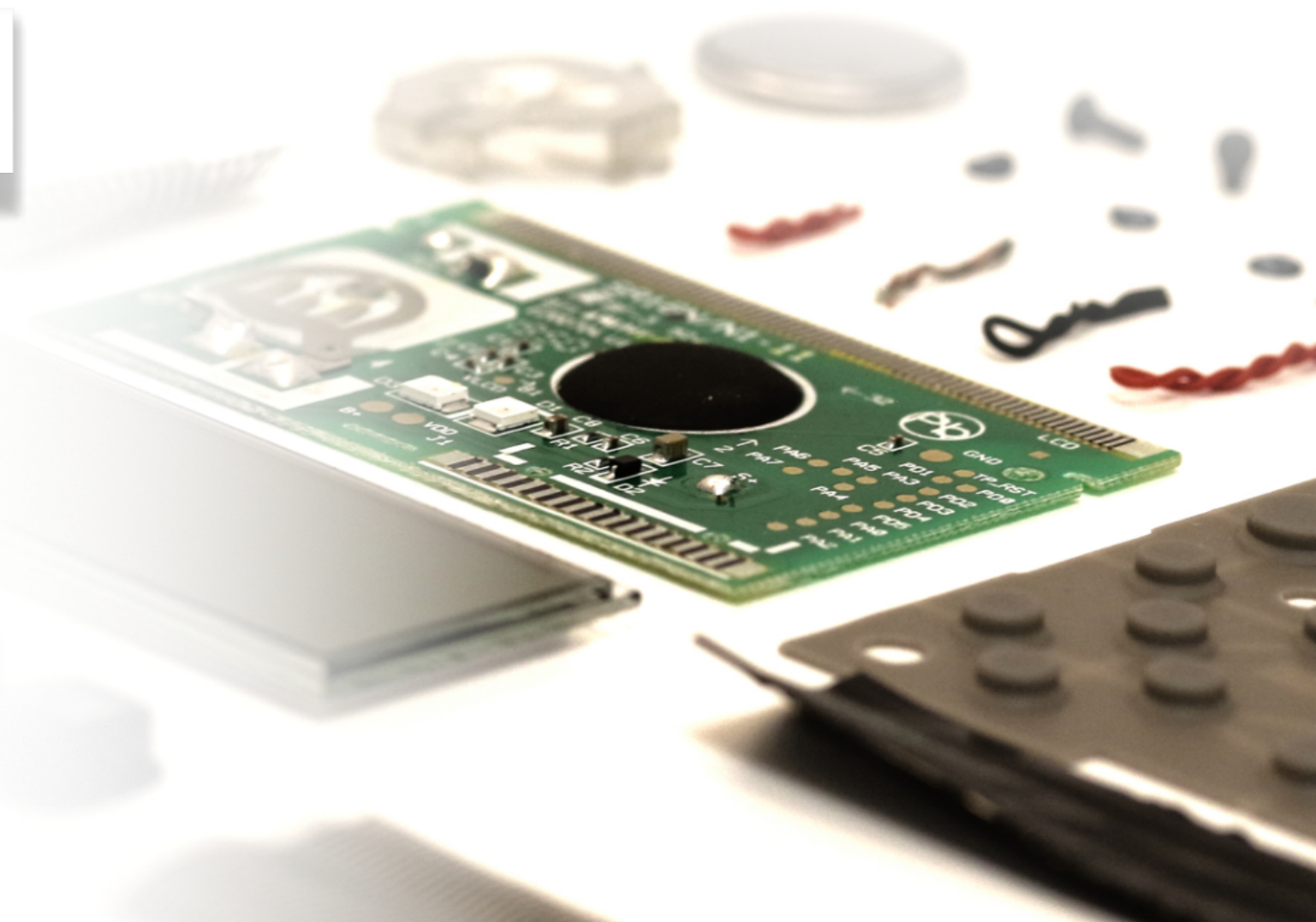
Webinar - New EU MDR CMRs and Allergens

Preparing for 50 new in-scope substances by 2028

The biggest update ever

Presented by:
Bruce Calder
VP Consulting

April 8 2026



Overview - Agenda

- EU MDR
 - CMRs
 - Allergens
 - Allergens
 - New allergens
 - EU MDR test issues
 - Biological Evaluation Plan
- CMRs
 - ATP 23
 - ATP 24
- Summary
- Updating tested devices
- Q&A



- **Claigan has completed EU MDR**
 - 10.4 Carcinogens, Mutagens, Reproductive Toxins (CMRs)
 - 23.4 (s) Allergens
- **For over 2,500 medical devices**
- **Claigan is world expert on this topic**

EU MDR and CMRs

- **Section 10.4 of EU Medical Device Regulation**

- Carcinogens, mutagens, and reproductive toxins (CMRs)
- In the invasive, fluid, or gas path
- Over 0.1% w/w

- **Are required to be**

- Identified
- Labelled
- Justified

10.4.1. Design and manufacture of devices

Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks posed by substances or particles, including wear debris, degradation products and processing residues, that may be released from the device.

Devices, or those parts thereof or those materials used therein that:

- are invasive and come into direct contact with the human body,
- (re)administer medicines, body liquids or other substances, including gases, to/from the body, or
- transport or store such medicines, body fluids or substances, including gases, to be (re)administered to the body,

shall only contain the following substances in a concentration that is above 0,1 % weight by weight (w/w) where justified pursuant to Section 10.4.2:

- substances which are carcinogenic, mutagenic or toxic to reproduction ('CMR'), of category 1A or 1B, in accordance with Part 3 of Annex VI to Regulation (EC) No 1272/2008 of the European Parliament and of the Council ⁽¹⁾, or
- substances having endocrine-disrupting properties for which there is scientific evidence of probable serious effects to human health and which are identified either in accordance with the procedure set out in Article 59 of Regulation (EC) No 1907/2006 of the European Parliament and of the Council ⁽²⁾ or, once a delegated act has been adopted by the Commission pursuant to the first subparagraph of Article 5(3) of Regulation (EU) No 528/2012 of the European Parliament and the Council ⁽³⁾, in accordance with the criteria that are relevant to human health amongst the criteria established therein.

10.4.2. Justification regarding the presence of CMR and/or endocrine-disrupting substances

The justification for the presence of such substances shall be based upon:

- an analysis and estimation of potential patient or user exposure to the substance;
- an analysis of possible alternative substances, materials or designs, including, where available, information about independent research, peer-reviewed studies, scientific opinions from relevant scientific committees and an analysis of the availability of such alternatives;
- argumentation as to why possible substance and/ or material substitutes, if available, or design changes, if feasible, are inappropriate in relation to maintaining the functionality, performance and the benefit-risk ratios of the product; including taking into account if the intended use of such devices includes treatment of children or treatment of pregnant or breastfeeding women or treatment of other patient groups considered particularly vulnerable to such substances and/or materials; and
- where applicable and available, the latest relevant scientific committee guidelines in accordance with Sections 10.4.3. and 10.4.4.

Also includes Endocrine Disruptors (Health)

But pretty overlapping with repr. toxins

EU MDR Justification Document Full Webinar



- **Claigan has a full [webinar](#) on the EU MDR Justification Document**

CLAIGAN ENVIRONMENTAL

CONSULTING

TESTING

SERVICES ▾

WEBINARS ▾

The video player shows a webinar titled "Claigan Webinar - A Practical Walkthrough of an EU MDR Justification Document" by Claigan Environmental. The video features the Claigan logo and the tagline "Less Journey. More Results." The presenter is Bruce Calder, VP Consulting, and the video was recorded on February 26, 2026. The video player includes a play button, a progress bar at 0:01 / 58:37, and a share icon. The video is set against a background of various medical devices and components.

All of Claigan past webinars can be found on

Our [website](#)

Or on [Youtube](#)

Minnesota PFAS PRISM Reporting



New Substances in 2026



EU MDR and Allergens

- **Section 23.4 (s)**
 - Information for user on
 - Sensitizers and allergens

23.4. Information in the instructions for use

The instructions for use shall contain all of the following particulars:

- (s) information that allows the user and/or patient to be informed of any warnings, precautions, contra-indications, measures to be taken and limitations of use regarding the device. That information shall, where relevant, allow the user to brief the patient about any warnings, precautions, contra-indications, measures to be taken and limitations of use regarding the device. The information shall cover, where appropriate:
 - precautions related to materials incorporated into the device that contain or consist of CMR substances or endocrine-disrupting substances, or that could result in sensitisation or an allergic reaction by the patient or user;

- **Includes**
 - Patients and
 - Healthcare practitioners

What are CMRs

- **Classified under the**
 - **Classification, Labelling and Packaging** of chemicals [regulation](#) (**CLP**)
- **EU MDR is only concerned with**
 - CLP harmonized classifications of
 - Cat I CMRs
- **The classifications under CLP are updated**
 - ~Annually
 - Under the **A**daptation to **T**echnical (*and scientific*) **P**rogress (**ATP**)

ATP Updates to CMR

- **ATP 23**
 - [Published](#) June 6 2025
 - In effect - February 2027
 - Twenty-two (22) new classifications
 - Eleven (11) are new Cat I CMRs
 - **Two (2) are high risk in medical devices**



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2025/1222

20.6.2025

COMMISSION DELEGATED REGULATION (EU) 2025/1222

of 2 April 2025

amending Regulation (EC) No 1272/2008 of the European Parliament and of the Council as regards the harmonised classification and labelling of certain substances

(Text with EEA relevance)

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 - Expected to be published ~July 2026
 - *WTO [Notification](#) occurred in Dec 2025*
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Brussels, XXX
[...] (2025) XXX draft

ANNEX

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to the

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EU MDR Allergens

- Historical the allergens handled for medical devices were
 - **Latex (natural latex proteins)**
 - **Nickel**
- Scientific knowledge has progressed significantly
 - **And so have reports of adverse events related to allergens**

EU MDR Allergens

Well Recognized Allergens

- Claigan allergen criteria
 - **Known allergen in medical devices**
 - **At least two (2) published sources**

Allergens Additions

Adhesives

- Common EU Medical Device Allergens**

Building block of PMMA

Acrylates

	CAS #	Allergen In Medical Devices?	Reference 1	Reference
Methyl Methacrylate (MMA)	80-92-6	Yes	https://www.mdpi.com/2079-928	https://ndl.ethernet.edu.et/bitstre
Lauryl Methacrylate	142-90-5	Yes	https://onlinelibrary.wiley.com/dc	https://link.springer.com/rwe/10.
Isobornyl Acrylate (IBOA)	5888-33-5	Yes	https://link.springer.com/article/1	https://journals.sagepub.com/do
Ethylene Glycol Dimethacrylate (EGDMA)	97-90-5	Yes	https://onlinelibrary.wiley.com/dc	https://ndl.ethernet.edu.et/bitstre
2-Octyl Cyanoacrylate	133978-15-1	Yes	https://academic.oup.com/cj/la	https://cdn-uat.mdedge.com/files
Ethyl Cyanoacrylate	7085-85-0	Yes	https://onlinelibrary.wiley.com/dc	https://journals.sagepub.com/do
2-Hydroxyethyl Methacrylate (2-HEMA)	212-782-2	Yes	https://onlinelibrary.wiley.com/dc	https://onlinelibrary.wiley.com/dc
2-Ethylhexyl Acrylate (2-EHA)	103-11-7	Yes	https://onlinelibrary.wiley.com/dc	https://ndl.ethernet.edu.et/bitstre
Cobalt	7440-48-4	Yes	https://pubmed.ncbi.nlm.nih.gov	https://www.sciencedirect.com/s
Hexavalent chromium	18540-29-9	Yes	https://link.springer.com/chapter	https://www.sciencedirect.com/s

Loctite

Metals

Allergens Additions

- Common EU Medical Device Allergens**

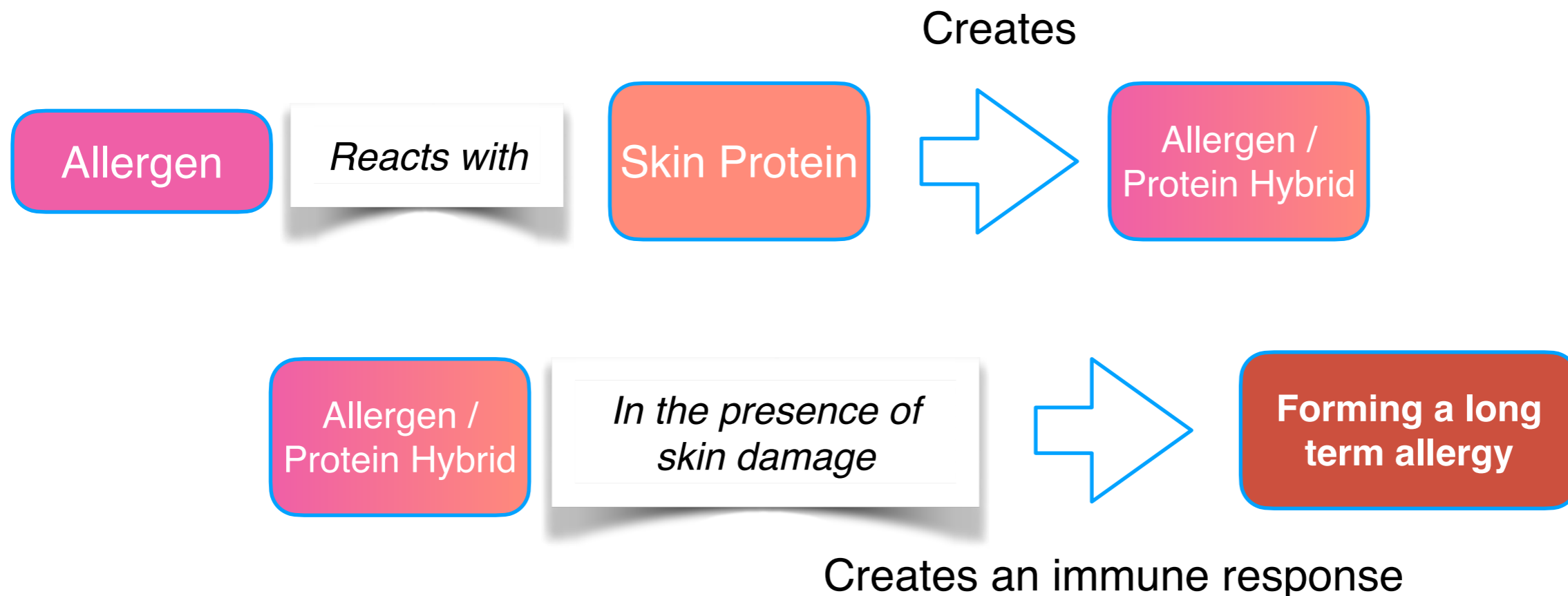
Substance	CAS #	Allergen In Medical Devices?	Reference 1	Reference 2
Methyl Methacrylate (MMA)	80-62-6	Yes	https://www.mdpi.com/2079-928	https://ndl.ethernet.edu.et/bitstre
Lauryl Methacrylate	142-90-5	Yes	https://onlinelibrary.wiley.com/dc	https://link.springer.com/rwe/10.
Isobornyl Acrylate (IBOA)	5888-33-5	Yes	https://link.springer.com/article/1	https://journals.sagepub.com/do
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Ethyl Cyanoacrylate	7085-85-0	Yes	https://onlinelibrary.wiley.com/dc	https://journals.sagepub.com/do
2-Hydroxyethyl Methacrylate (2-HEMA)	212-782-2	Yes	https://onlinelibrary.wiley.com/dc	https://onlinelibrary.wiley.com/dc
2-Ethylhexyl Acrylate (2-EHA)	103-11-7	Yes	https://onlinelibrary.wiley.com/dc	https://ndl.ethernet.edu.et/bitstre
Cobalt	7440-48-4	Yes	https://pubmed.ncbi.nlm.nih.gov	https://www.sciencedirect.com/s
Hexavalent chromium	18540-29-9	Yes	https://link.springer.com/chapter	https://www.sciencedirect.com/s

Published References

Allergens and Medical Devices

- Medical device allergic reactions are primarily
 - Allergic contact dermatitis (ACD)

- **Mechanism**



Compete Failure of Standard EU MDR Tests

- **None of the following tests are effective for these allergens**

- ~~DPPRA (Direct Peptide Reactivity Assay - KE1)~~ *Covalent bonds only*

- ~~KeratinoSens (KE2)~~ *Wrong receptors*

- ~~h-CLAT (Human Cell Line Activation Test - KE3)~~ *Optimized for the wrong allergens*

THP-1 cells cannot metabolically "activate" the pro-hapten

- Plus the standard version of each is aqueous, not oil based

Compete Failure of Standard EU MDR Tests

- **None of the following tests are effective for these allergens**

- ~~DPPRA (Direct Peptide Reactivity Assay - KE1)~~ *Covalent bonds only*

Metal Allergens

Ni, Co

Coordination complexes

Not covalent bonds

Allergen / Protein Hybrid

KE1 does not work

Acrylic Allergens

MMA, IBOA

Steric Hindrance

Very slow reacting to proteins

Allergen / Protein Hybrid

Create a false negative for KE1

Compete Failure of Standard EU MDR Tests

- **None of the following tests are effective for these allergens**

- ~~KeratinoSens (KE2)~~ *Wrong receptors*
- ~~h-CLAT (Human Cell Line Activation Test - KE3)~~ *Optimized for the wrong allergens*

Metal Allergens

Ni, Co

Wrong receptors

No TLR4

KE2 and KE3 do not work

Neither do animal tests, btw

Acrylic Allergens

MMA, IBOA

Needs oil

Standard tests are aqueous

KE2 and KE3 do not work

Neither do animal tests, btw

Reminder on Standard EU MDR Tests

- **None of the following tests are effective for these allergens**

- ~~DPPRA (Direct Peptide Reactivity Assay - KE1)~~

*Covalent
bonds only*

- ~~KeratinoSens (KE2)~~

Wrong receptors

- ~~h-CLAT (Human Cell Line Activation Test - KE3)~~

*Optimized for the
wrong allergens*

- **Some (of many) references**

- [OECD Test Guideline No. 442C: In Chemico Skin Sensitisation: Direct Peptide Reactivity Assay \(DPPRA\)](#)

- [EURL ECVAM: Direct Peptide Reactivity Assay \(DPPRA\) Validation Study Report \(2012 / TSAR\)](#)

- [Peptide reactivity assays for skin sensitisation – scope and limitations](#)

- [OECD Test Guideline No. 442D: In Vitro Skin Sensitisation: ARE-Nrf2 Luciferase Test Method \(KeratinoSens™\)](#)

- [Non-animal methods to predict skin sensitization \(I\): the Cosmetics Europe database.](#)

- [OECD Test Guideline No. 442E: In Vitro Skin Sensitisation: In Vitro Skin Sensitisation assays](#)

[Extraction With Sweat-Sebum Emulsion as a New Test Method for Leachables in Patch-Based Medical Devices, Illustrated by Assessment of Isobornylacrylate \(IBOA\) in Diabetes Products](#)

Allergen Test Issues

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Biological Evaluation Plan (BEP) Allergens



- **What should your BEP look like?**
 1. Identify high risk materials for allergens
 - *Example - adhesives and acrylic polymers (like PMMA)*
 - *Example - steel (for Ni, Co, and Cr6+)*
 2. Test for content
 - *Is the allergen present?*
 3. If present, use standard allergen tests based on exposure
 - *Casual contact - wipe test*
 - *Prolonged contact - soak test (such as EN 1811)*
 - *If organic, use **sweat / sebum mixture***

Biological Evaluation Plan (BEP)

Allergens



- **Why not just use ISO 10993-18**
 1. Not structured for organic allergens
 - *Ethanol / water is not effective for acrylates*
 2. Poor calibration
 - *ISO 10993-18 using 'open library' matching*
 - *Not substance based calibration*
 - *Almost all organic substances reported are 'maybes'*
 3. Very expensive
 - *50X the cost of doing the testing properly*
 4. And you will likely have to redo the test after if you get a positive

EU MDR Allergens

Acrylates

- Main presences
 - Sticker (adhesives)
 - Acrylic polymers
 - *Examples - PMMA, plexiglass*



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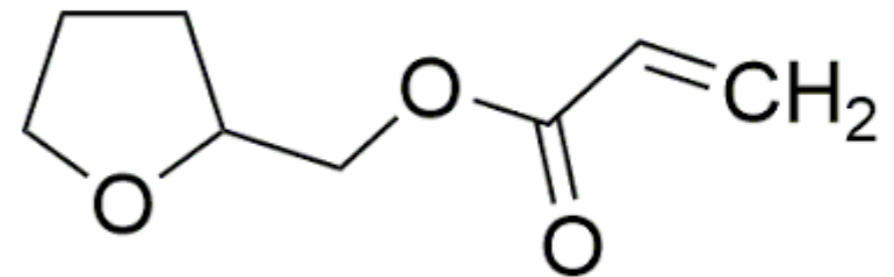
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ATP 23 - High Risk Substance

Tetrahydrofurfuryl methacrylate

- Tetrahydrofurfuryl methacrylate (THFMA) - CAS # 2455-24-5

- Repr. IB



- Common uses are as a copolymer in

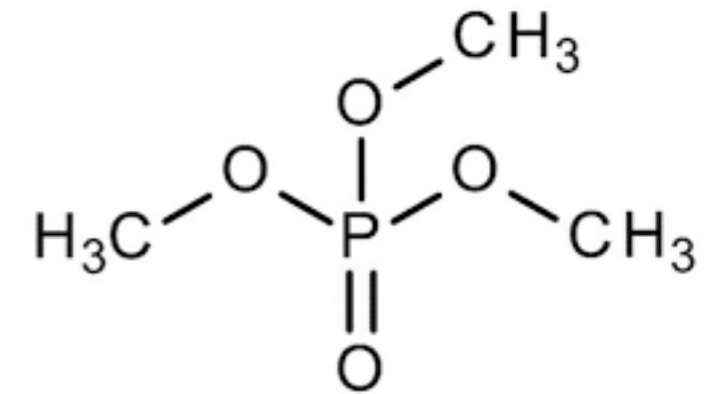
- Dental Composites and Resins
- Biomedical 3D Printing
- Medical Adhesives



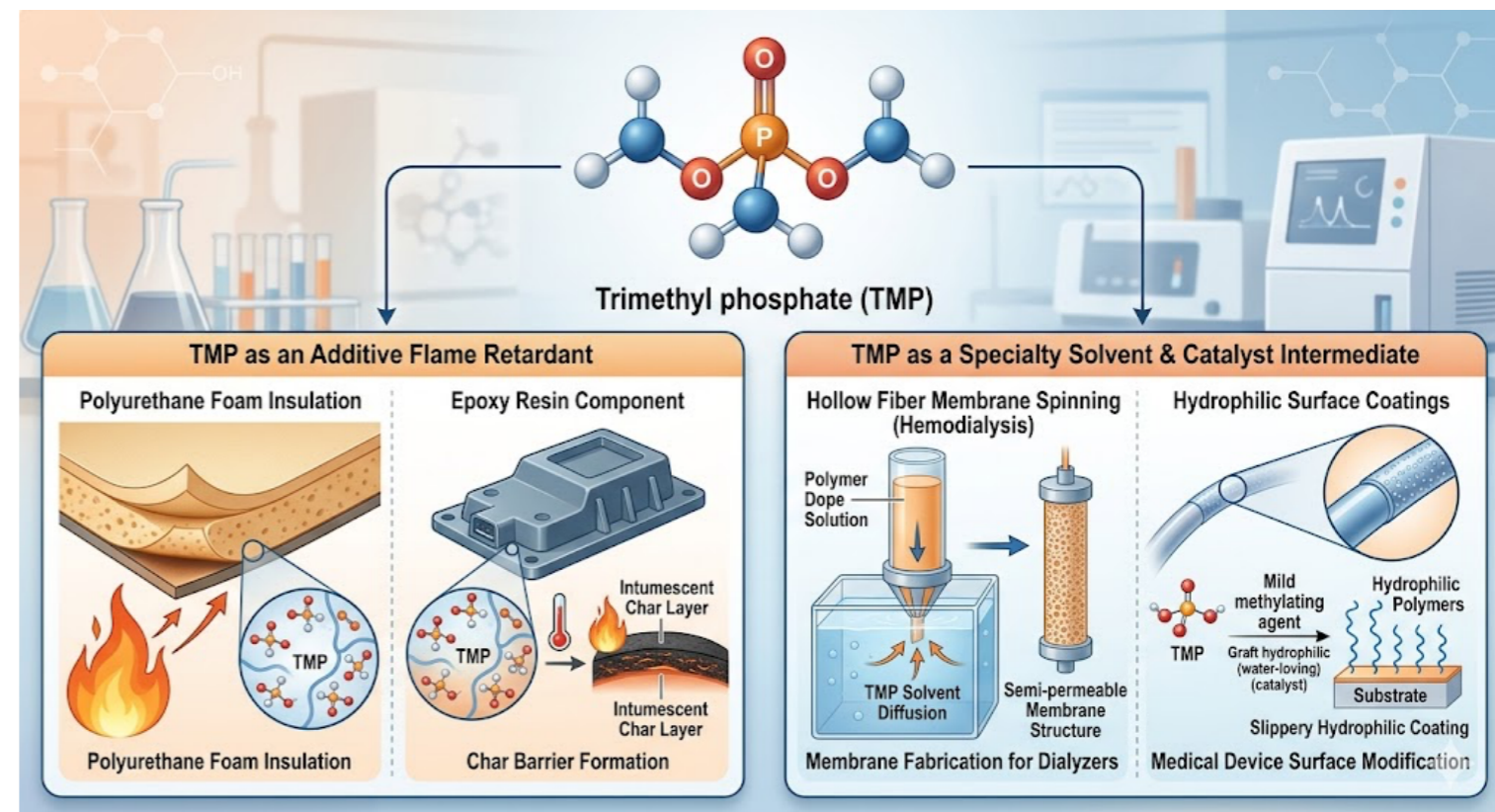
ATP 23 - High Risk Substance

Trimethyl Phosphate

- Trimethyl Phosphate(TMP) - CAS # 512-56-1
- Mut. 1B, Cat 1B, Repr. 1B



- Common uses are varied
 - Solvent in hollow fiber membranes
 - Surface coating
 - Flame retardant



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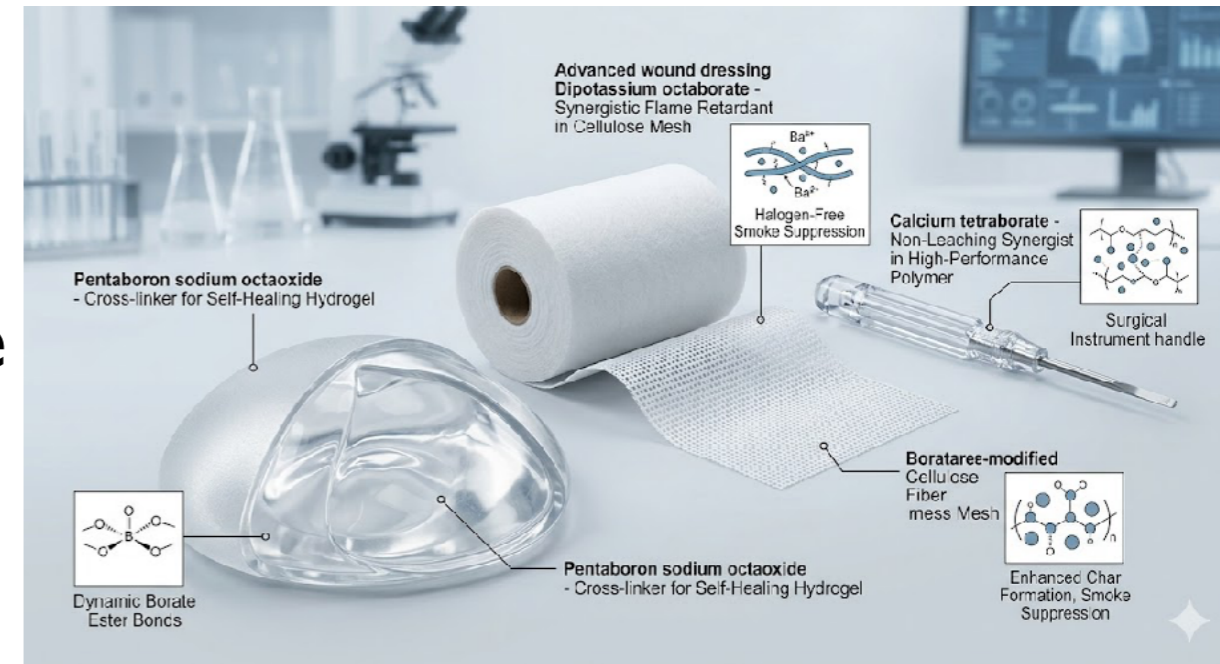
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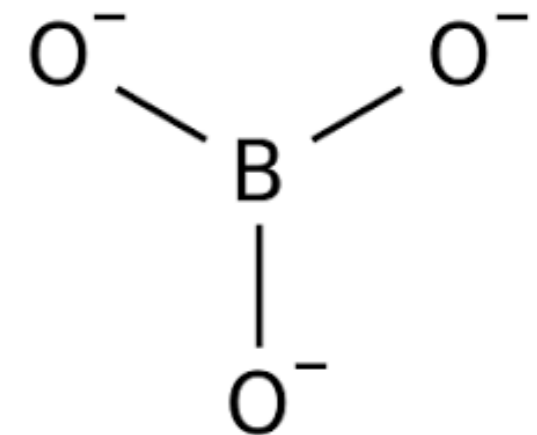
ATP 24 - High Risk Substance(s)

Borates

- Borates
 - Repr. 1B (3,000 ppm)
 - Pentaboron sodium octaoxide
 - Dipotassium octaborate
 - Calcium tetraborate



- Common uses
 - Synergists for halogen free flame retardants
 - Cellulose based materials (flame retardant)
 - Hydrogels



ATP 24 - High Risk Substance(s)

Bromides



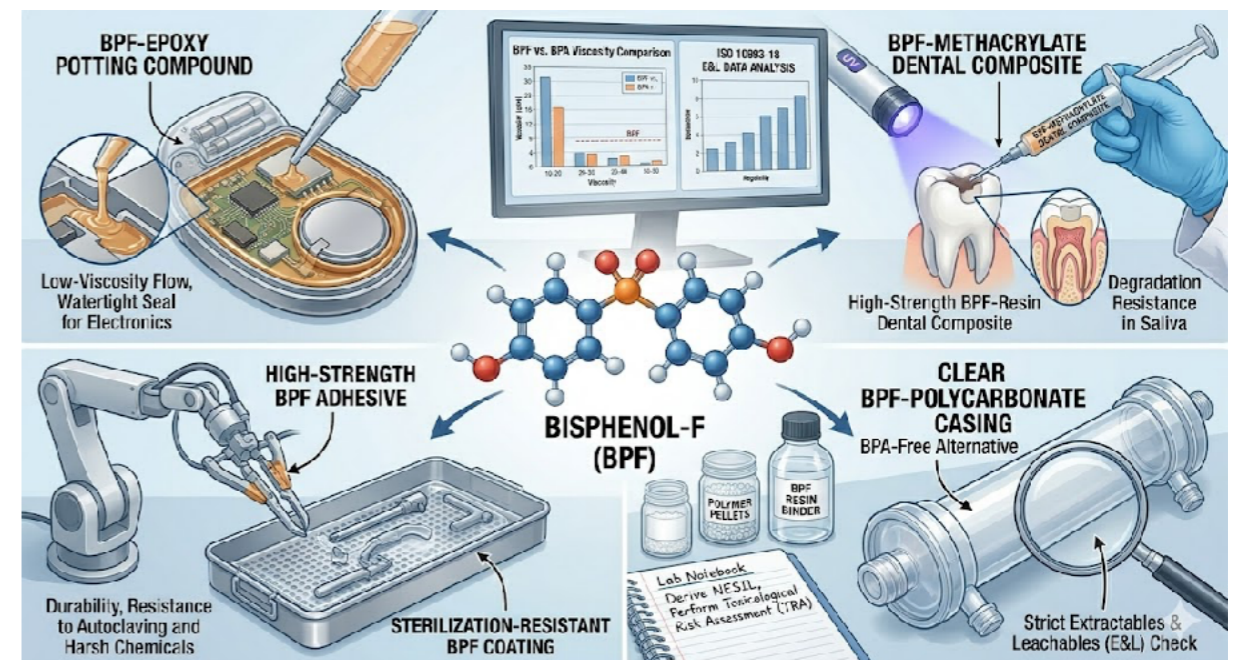
- Bromides
 - *Repr. IB (3,000 ppm)*
 - Potassium bromide
 - Calcium bromide

- Common (*ish*) uses
 - Flame retardant - transparent polycarbonate

ATP 24 - High Risk Substance(s)

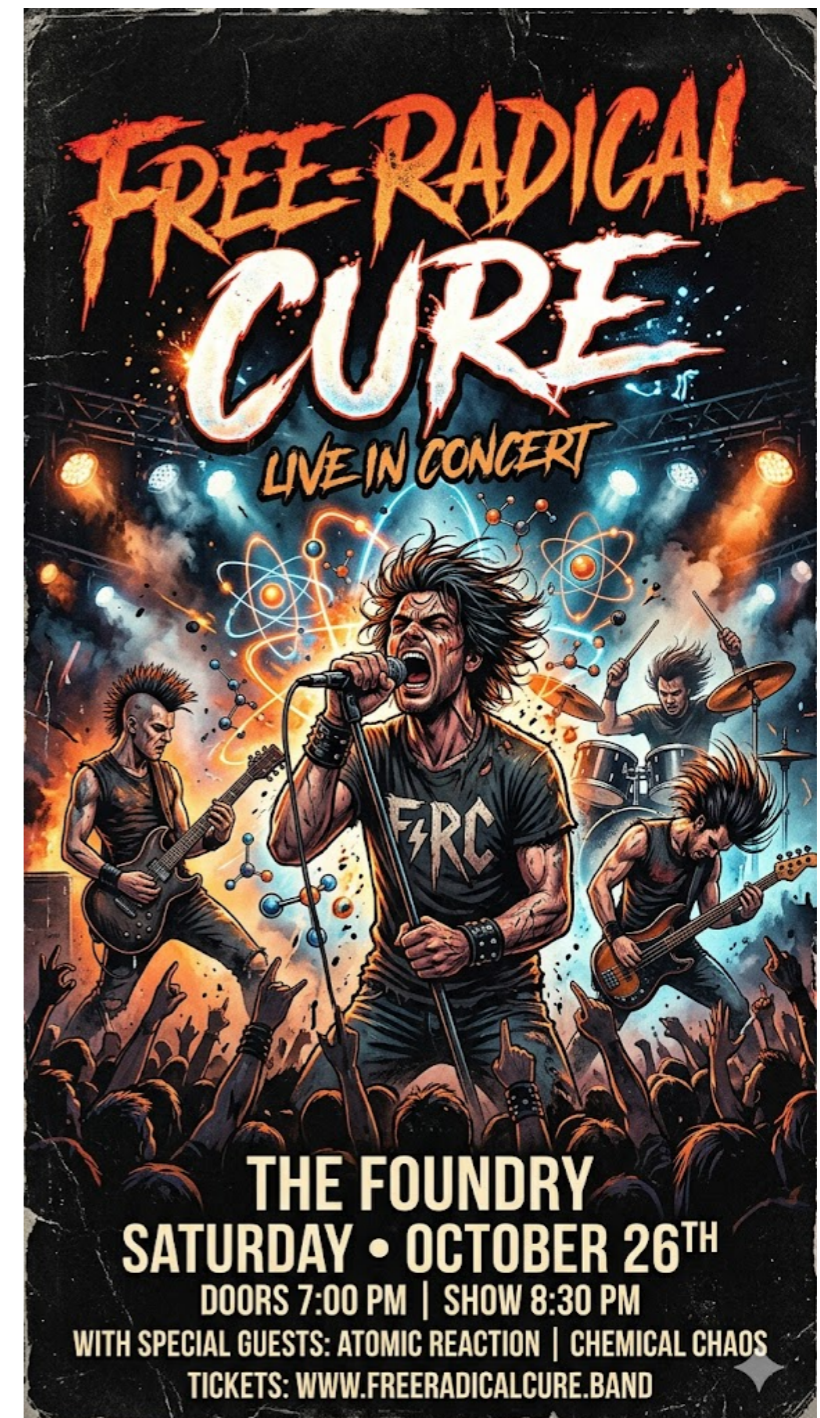
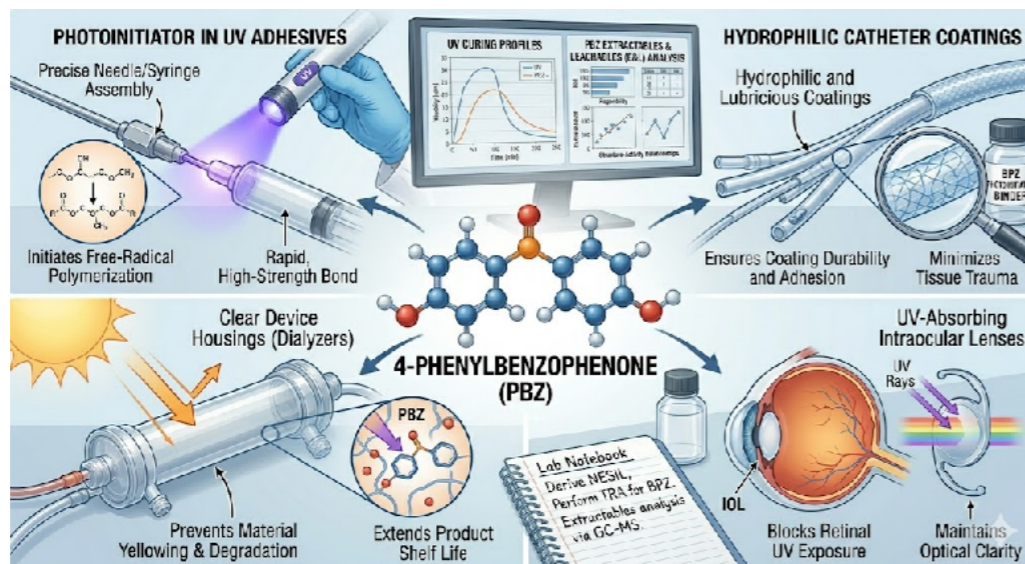
Bisphenol F

- Bisphenol F - CAS# 620-92-8
 - *Repr. IB*
- Common uses
 - Bisphenol A free 'polycarbonate' and epoxy
 - Dental composites



ATP 24 - High Risk Substance(s) 4-phenylbenzophenone (PBZ)

- 4-phenylbenzophenone (PBZ) - CAS# 2128-93-0
 - Repr. / B
- Common uses (very common)
 - UV curing acceleration for
 - Free-Radical Curing
 - UV cured acrylics

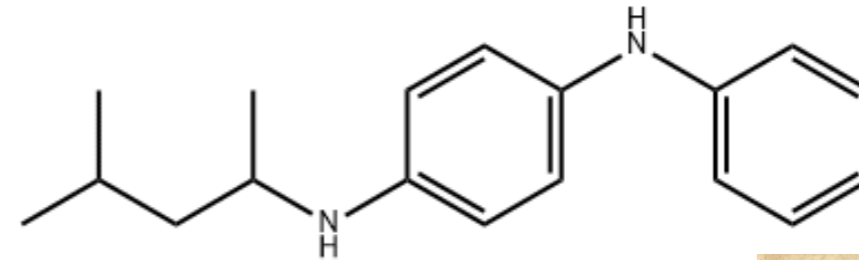


ATP 24 - High Risk Substance(s)

N-1,3-dimethylbutyl-N'-phenyl-p-phenylenediamine

- N-1,3-dimethylbutyl-N'-phenyl-p-phenylenediamine (6PPD)

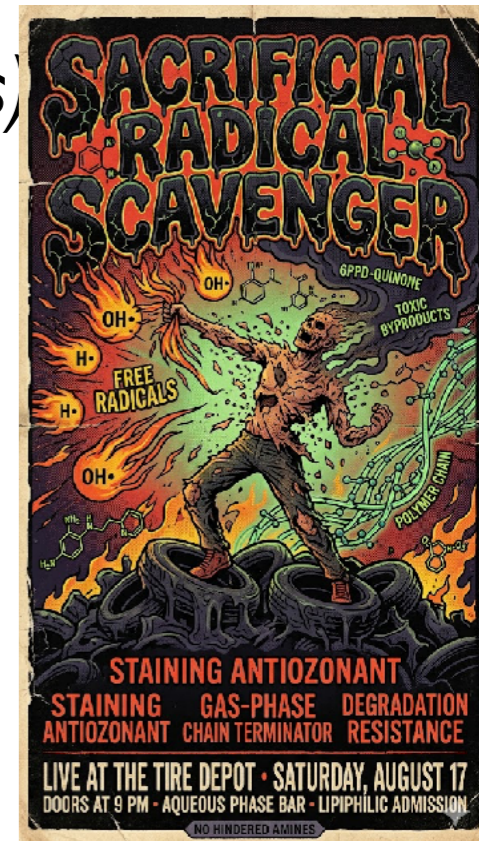
- *Repr. 1B*



- Common uses (*but very less common in medical devices*)

- Anti-oxidant in nitrile rubber

- 6PPD is a “Sacrificial Radical Scavenger”
- Sacrifices itself by reacting to ‘radicals’



- Less common in medical devices because of its significant migration / leaking

Allergens Additions

Adhesives

- Common EU Medical Device Allergens**

Building block of PMMA

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Hexavalent chromium	18540-29-9	Yes	https://link.springer.com/chapter	https://www.sciencedirect.com/s

Loctite

Metals

Updated

- **None of the following tests are effective for these metal allergens**

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THP-1 cells cannot metabolically "activate" the pro-hapten

Plus the standard version of each is aqueous, not oil based

- Ultimately, this is why regulatory documents like OECD TG 442E explicitly warn that the h-CLAT has limitations with pro-haptens and chemicals with a $\text{LogKow} > 3.5$.
- Relying on KE3 to clear an acrylic medical device without supporting analytical chemistry is a **massive regulatory risk**.

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 - 10.4 Carcinogens, Mutagens, Reproductive Toxins (CMRs)
 - 23.4 (s) Allergens
- **For over 2,500 medical devices**
- **Claigan is world expert on this topic**

**Claigan has a straight forward UPDATE
PROCESS for previously tested
devices**

Updating Previously Tested Products

- **Allergens**

- Acrylics would have been identified in original testing
- Cobalt and hex chrome would have been included in original testing

- **CMRs**

- Testing data would include screening data for
 - Bisphenol-F
 - 6PPD
 - PBZ
 - TMP
 - Borates
 - Bromides

- **Contact us about an update**

Biological Evaluation Plan (BEP) Allergens



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Q&A