PQRI 2023 Webinar

PFAS Restrictions – What you Need to Know and the Potential Impact Across the Pharmaceutical Industry and the Supply Chain Continuum

August 8, 2023

Housekeeping

- All Attendees are on mute.
- Webinar is recorded and will be posted on the PQRI website.

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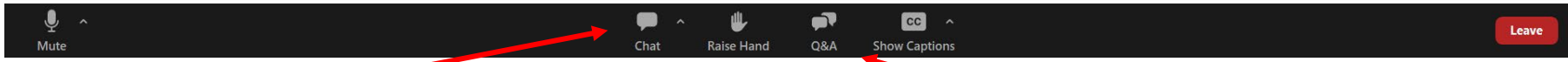
August 8, 2023



• The Chat function has been disabled for Attendees. Type your question in the Q&A box.

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Agenda

- Introduction to PFAS / Potential Impact Across the Pharmaceutical Industry (15 min)
  - Diane Paskiet, West Pharmaceutical Services
- PQRI Questionnaire – Preliminary Results (10 min)
  - Cheryl Stults, C & M Technical Consulting, LLC
- Assessment of Impact of PFAS Ban and Planning Ahead (30 min)
  - Pharma Perspective
    - Atish Sen, AstraZeneca
  - CDMO Perspective
    - Helen Derbyshire, Kindeva
  - Supplier Perspective
    - Quintin Lai, West Pharmaceutical Services
- Q&A /Moderated Discussion (45 min)

  Above speakers and Rik Lostritto, Consultant

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Product Quality Research Institute (PQRI)

What is PQRI? *A neutral form for regulators and industry to advance pharmaceutical regulations, standards and science.*

Mission:

PQRI is a non-profit consortium of organizations, including standard setting and regulatory agencies working together to generate and share timely, relevant, and impactful information that advances drug product quality, manufacturing, and regulation.

FDA U.S. FOOD & DRUG ADMINISTRATION

usp

Health Canada

PDA Parenteral Drug Association

IPEC AMERICAS — International Pharmaceutical Excipients Council

IPAC-RS International Pharmaceutical Aerosol Consortium on Regulation & Science

ELSIE Extractables and Leachables Safety Information Exchange

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What Does PQRI Do ?

- Unites thought leaders from regulatory agencies, standard setting bodies, industry and academia to conduct research and share knowledge on emerging scientific and regulatory quality challenges
- Provides a unique, neutral forum to develop common understandings of current scientific, technical and regulatory challenges among a diverse collection of industry organizations and FDA and other regulatory bodies
- Creates opportunities to accomplish mutual goals that cannot be achieved by individual organizations
- Impacts global regulatory guidance and standards, bringing maximum value to members and patients

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Introduction to PFAS / Potential Impact Across the Pharmaceutical Industry

Presented by Diane Paskiet, West Pharmaceutical Services

August 8, 2023

EU Proposed Restrictions
Per and Polyfluoroalkyl Substances (PFAS)

The Netherlands, Germany, Denmark, Sweden, Norway

PFAS Position Paper and Questionnaire

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Background: EU Chemical Legislation

- **REACH[1] Registration, Evaluation, Authorization and Restriction of Chemicals**
  - **Phases out or restricts substances of very high concern (SVHC).**
    - Any substance found to be carcinogenic (C), mutagenic (M) or toxic (T) to reproductive(R) health
    - Substances that are persistent(P), bioaccumulate (B) and toxic(T) or is very persistent (vP)
- **Annex XV: Dossiers - RESTRICTION REPORT: PROPOSAL FOR A RESTRICTION**
  - **Annex XVII:** Restrictions on the manufacture, placing on the market and use of certain dangerous substances, mixtures and articles
  - **Annex XIV:** List of substances subject to authorization
- **ECHA[2] (European Chemical Agency)**
  - Coordinates evaluations of chemical hazards, public consults and manages chemical databases.

1.Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006, concerning the Registration, Evaluation, Authorization and Restriction of Chemicals, as amended

2. Organization that implements the EU's chemicals legislation to protect health and the environment https://echa.europa.eu/about-us

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ECHA Proposed Restriction

- PFAS are regulated as a chemical class or as sub-groups, based on their intrinsic properties:
  - Persistence, bioaccumulation, potential, toxicity, mobility and molecular size
- There are 2 restriction options:
  - A full ban with no derogations and a transition period of 18 months from EiF.
  - A full ban with use-specific time-limited derogations.(18-month transition period plus either a five- or 12-year derogation period).
- There are time-unlimited derogation for PFASs used as active substances in Human and Veterinary Medicinal Products (MP).
  - Addressed under their respective regulations

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Annex XV Report: https://echa.europa.eu/restrictions-under-consideration/-/substance-rev/72301/term

Stakeholder Consultation: Call for Evidence (CfE):

Questionnaire on all uses of PFAS

Acquire data to ensure the 5 competent authorities had correct information for the assessment and preparation of a REACH Annex XV Restriction Dossier.

October 2021

No data - No Derogations

- [ ] Cleaning agents, polishes, waxes (non-industrial uses)
- [ ] Cosmetics
- [ ] Food contact materials & packaging
- [ ] Lubricants
- [ ] Construction products
- [ ] Medical devices
- [ ] Medicinal products
- [ ] Metal plating & manufacturing of metal products
- [ ] PFAS production (manufacturing)
- [ ] Ski treatment
- [ ] TULAC (textiles, upholstery, leather, apparel and carpets)
- [ ] Petroleum & mining
- [ ] F-gases
- [ ] Electronics & energy
- [ ] Transportation
- [ ] Waste

Per Appendix G2 Stakeholder Consultation

CfE Data on PFAS Usage and Sub-usage

- PFAS Manufacturing
  - (Fluoropolymers process aids)
- Medical Devices
  - Implants, Guide Wires, Catheters, Mesh, Cannulas, Packaging, Inhalers/Propellants
- Consumer Mixtures
  - Cleaning Agents/Surfactants, Waxes/Polishes, Siloxanes
- Lubricants/Solvents
- Metal Plating
- Energy, Electronics and Semi-conductors
- Transportation
- Gases
- Textile, Upholstery, Apparel, Carpets (TULAC)
- Food Contact Materials and Packaging (FCM)
- Cosmetics
- Ski Treatment
- Construction Products
- Petroleum and Mining

Appendix E2:https://echa.europa.eu/registry-of-restriction-intentions/-/dislist/details/0b0236e18663449b

Per- and polyfluoroalkyl substances (PFAS)

ECHA PFAS Definition:

Any substance that contains at least one fully fluorinated methyl (CF_3-) or methylene (-CF_2-) carbon atom (without any H/Cl/Br/I attached to it).

Per OECD (Organization for Economic Co-operation and Development)

Other definitions exist in other countries, various standards, and literature

Scope:

Depends on molecular structure and structural similarity, and associate substances (salts, degradation products/precursors, and metabolites).

PFASs are very persistent themselves or degrade to form (short or long timescale) terminal degradation products which still contain one/several perfluoroalkyl moieties and very persistent.

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Annex XV Report: https://echa.europa.eu/restrictions-under-consideration/-/substance-rev/72301/term

PFAS Grouping Approach Triggers Hazards

- Risks are based on structural similarity (common perfluoroalkyl moieties) primarily related to the very persistent property of the substances.

Chemicals Strategy for Sustainability (CSS) EC:2020

Chemical Group

- Per and Polyfluoroalkyl Substances

Categories

- Non-Polymers
- Polymers

Classes

- Perfluoroalkyl Substances 
- Polyfluoroalkyl Substances 
- Fluoropolymers ★ 
- Polymeric Perfluoropolyether 
- Side chain Fluorinated Polymers 

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★ **Fluoropolymers are designated as (PLC) polymers of low concern by (OECD).**

Regulatory History: Per- and polyfluoroalkyl substances (PFAS)

Year	Substance	Status
2006	**PFOS**	**Restriction in POP regulation**
2012	C11-C14 PFCAs	Listed as vPvB
2013	C8 PFCA (PFOA +salts)	Listed as PBT
2015	C9 PFCA (PFNA + salts)	Listed as PBT
2016	C10 PFCA (PFDA +salts)	Listed as PBT
2017	C6 PFSA (PFHxS +salts	Listed as vPvB
2019	**TDFAs solvent based sprays**	**Annex XVII entry**
2019	TFHPA + salts and halides	Listed as Persistent, Mobile and Toxic
2020	**PFOA salts and related substances**	**Restriction in POP regulation**
2020	C4 PFSA (PFBS + salts)	Listed as ELoC
2021	**C9-C14 PFCAs**	**Annex XVII entry**
2021	**PFHxS and related substances**	**Proposal expected to be included in POP**
2022	**Aqueous Firefighting Foams**	**Proposal in preparation**
2022	PFHpA + salts	Listed as vPvB, PBT, ELoC
2023	**PFHxA + salts related substances**	**Proposal waiting for decision**

Dates continually updated

POP: Persistent Organic Pollutant Regulation that is banned from production or use in EU

ELoC: Equivalent Level of Concern to be regulated under REACH

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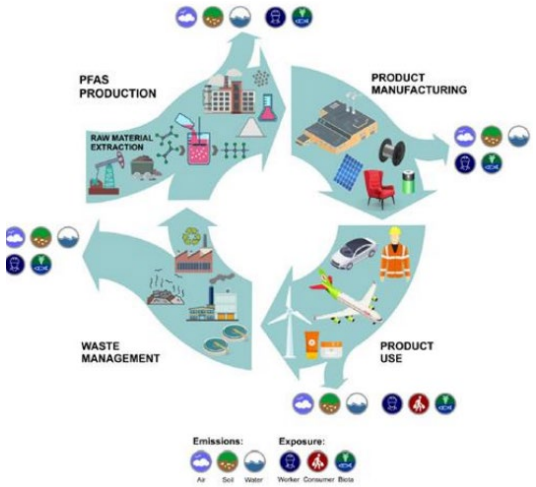
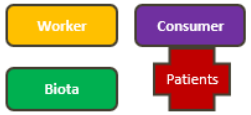
PFAS Lifecycle and Application

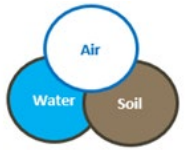
Annex A.1 PFAS Lifecyle EC 2020



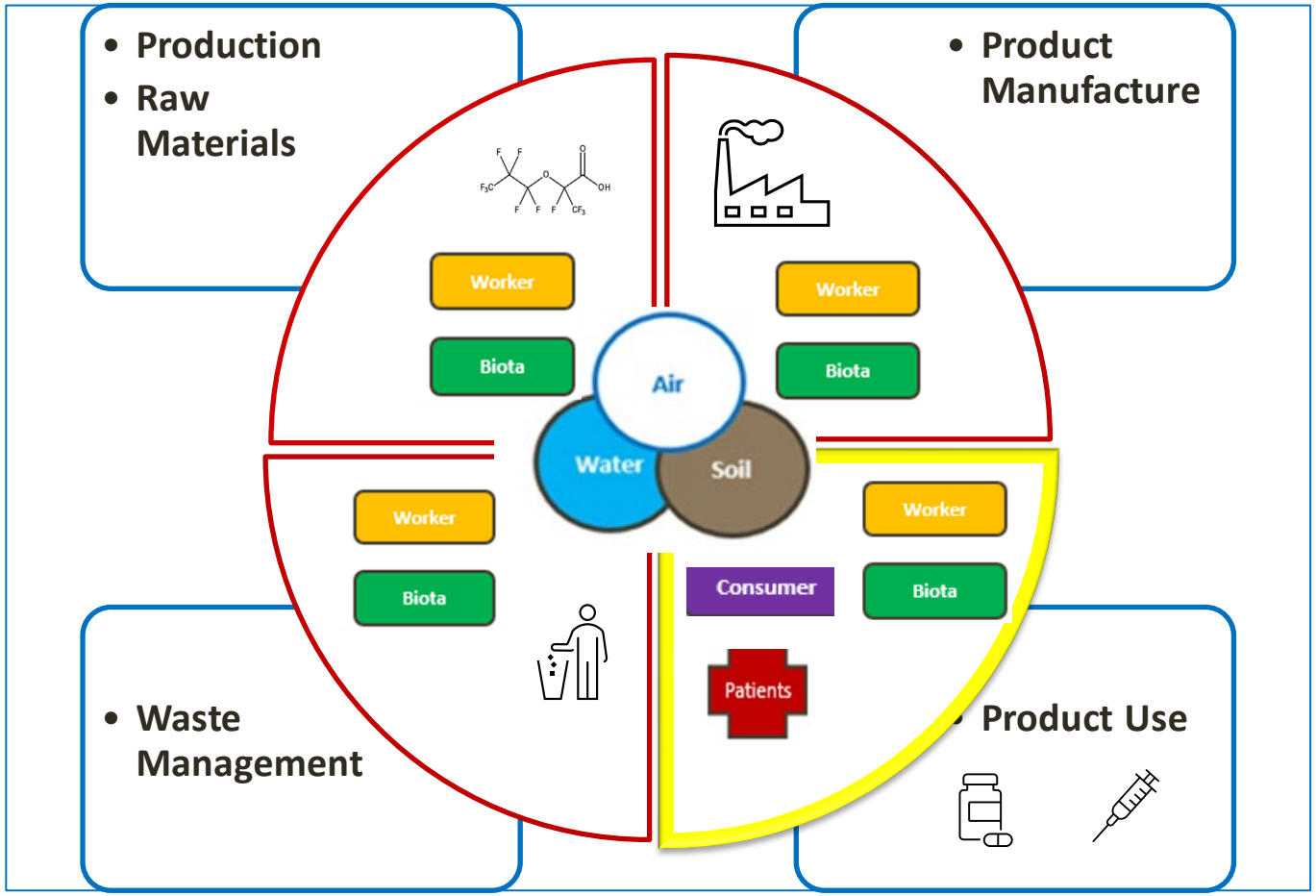
Exposure



Emissions



Considerations for Patient Health and Safety



PQRI Position Paper - Built on PQRI Questionnaire

- To understand PFAS dependencies and sources throughout pharmaceutical development and commercialization
- To connect drug product modalities with production of medicines associated with PFAS
  - Linking therapeutic areas, routes of administration, and impact to the prevention, treatment, or cure of noncommunicable and infectious diseases
- To understand medicinal supply chain and risks to patient populations
  - Realizing consequences to public health and well-being
- To convey responsible environmental initiatives and upstream innovation for development of alternatives and potential for technically feasible alternatives
  - Considering impact of increased costs and time for upstream and downstream development and validation
  - Recognizing regulatory approval of marketed and pipeline medicinal products

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ECHA Consult: Specific Information:

Addressed by PQRI Questionnaire

1. **Sectors and (sub-)uses**
   - **a. Medicinal Products Absent**
2. **Emissions in the end-of-life phase: environmental impact** (based on available literature)
   - a. Emissions across the different stages of the lifecycle of products
3. **Emissions in end-of-life phase: waste management**
   - a. % annual emissions and % wastes (based on available literature)
   - **b. Waste treatment: incineration, landfilling and recycling /form**
4. **Impacts on the recycling industry** (based on available literature)
   - a. technical and economic feasibility of recycling processes
5. **Proposed derogations – Tonnage and emissions** (based on available literature)
   - a. tonnage of PFAS used per year and resulting emissions to the environment and justifications

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ECHA Consult: specific information:

Addressed by PQRI Questionnaire

6. Missing uses – Analysis of alternatives and socio-economic analysis:

a. Type of PFAS and key functionalities for intended use
b. Suitable alternatives, likelihood of success and time expected for substitution
c. Tonnage/ emissions, #companies,costs, profits, employment ((based on available literature)

7. Potential derogations marked for reconsideration – Analysis of alternatives and socio-economic analysis:

a. Potential for technically and economically feasible alternatives
b. Inventory on the market at EiF and implemented before the transition period

8. Other identified uses – Analysis of alternatives and socio-economic analysis

a. Available evidence and key aspects for which derogation is potentially warranted
   i. **Medicinal Product/Pharmaceutical Sector**

a. **9. Degradation potential of specific PFAS sub-groups:** (reference literature)
   a. Further information regarding degradation pathways, kinetics ,metabolites

10. Analytical methods: (reference literature)

a. New or additional information on analytics not yet considered in the Annex XV

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PFAS Research & Gaps

- Opportunities across many sectors for reductions and eliminations of PFAS:
  - **Risk for unintended consequences with changes in practices or chemical substitutions**
  - **The path to PFAS reduction is not well-defined**
    - **Alternatives requires a complete understanding of properties for use prior to development.**
- Overarching major challenges around alternatives include:
  - **The lack of awareness of where PFAS are included in products and awareness of potential alternatives**.
  - **The lack of information about the toxicity associated with certain PFAS.**
  - **The possibility that certain non-fluorinated alternatives may not be less harmful, leading to substitution regret.**
  - **Technical challenges in identifying and implementing alternative products and processes**.

References

https://echa.europa.eu/en/restrictions-under-consideration/-/substance-rev/72301/term

- Annex XV: Restriction Report
- Annex A: Manufacture and Use
- Annex B: Information on Hazards and Risk
- Annex E: Impact Assessment
  - Appendix E2 Hazards and Assessments
  - Appendix E4 Analytical Methods
- Annex F: Assumptions Uncertainty and Sensitivities
- Annex G: Stakeholder Information
  - Appendix G1 Call for Evidence
  - Appendix G2 Stakeholder Consultation
- Information note on restriction report

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PQRI Questionnaire – Preliminary Results

Presented by Cheryl Stults, C&M Technical Consulting, LLC

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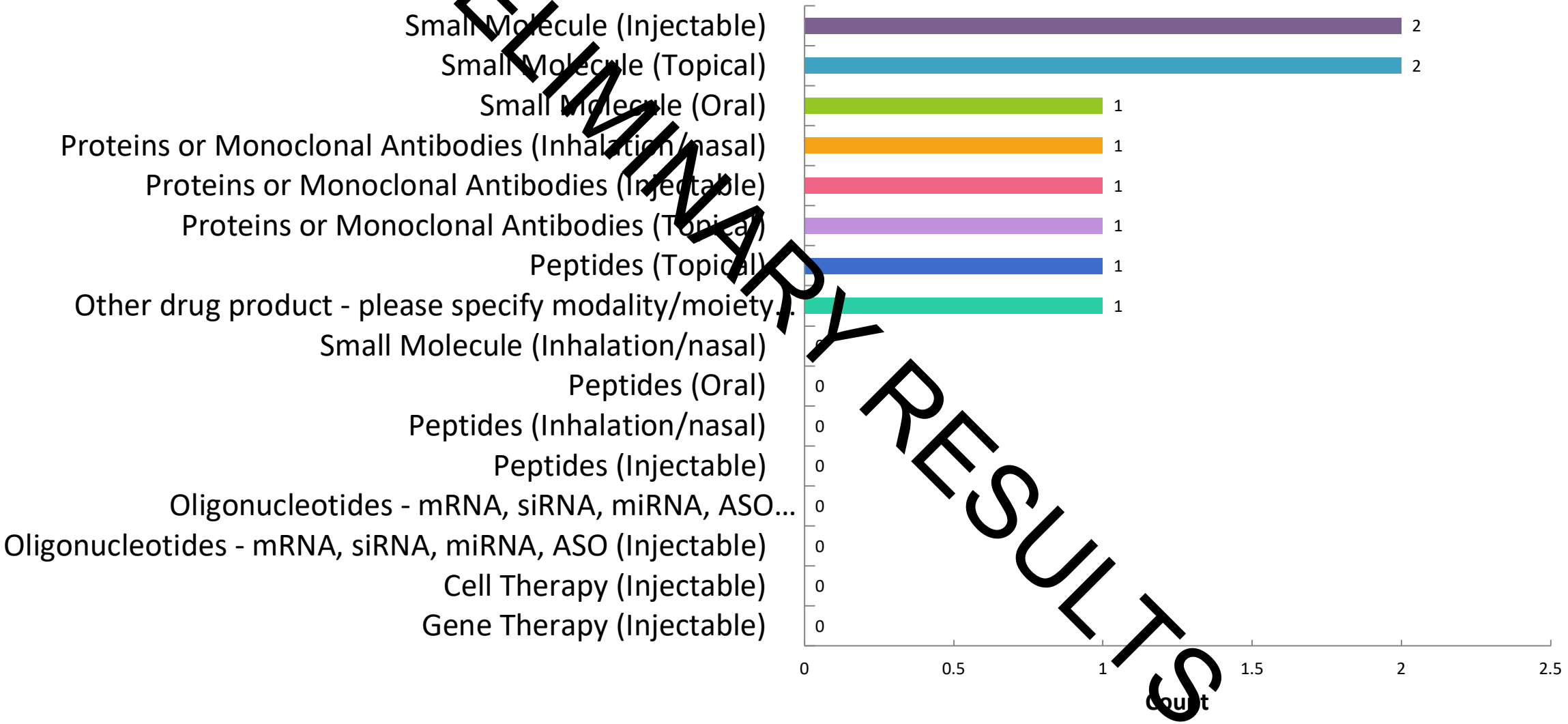
PHARMA Q:

Of the drug products that your organization manufactures or is developing, which of the following product types would be impacted by the PFAS ban being proposed by ECHA?

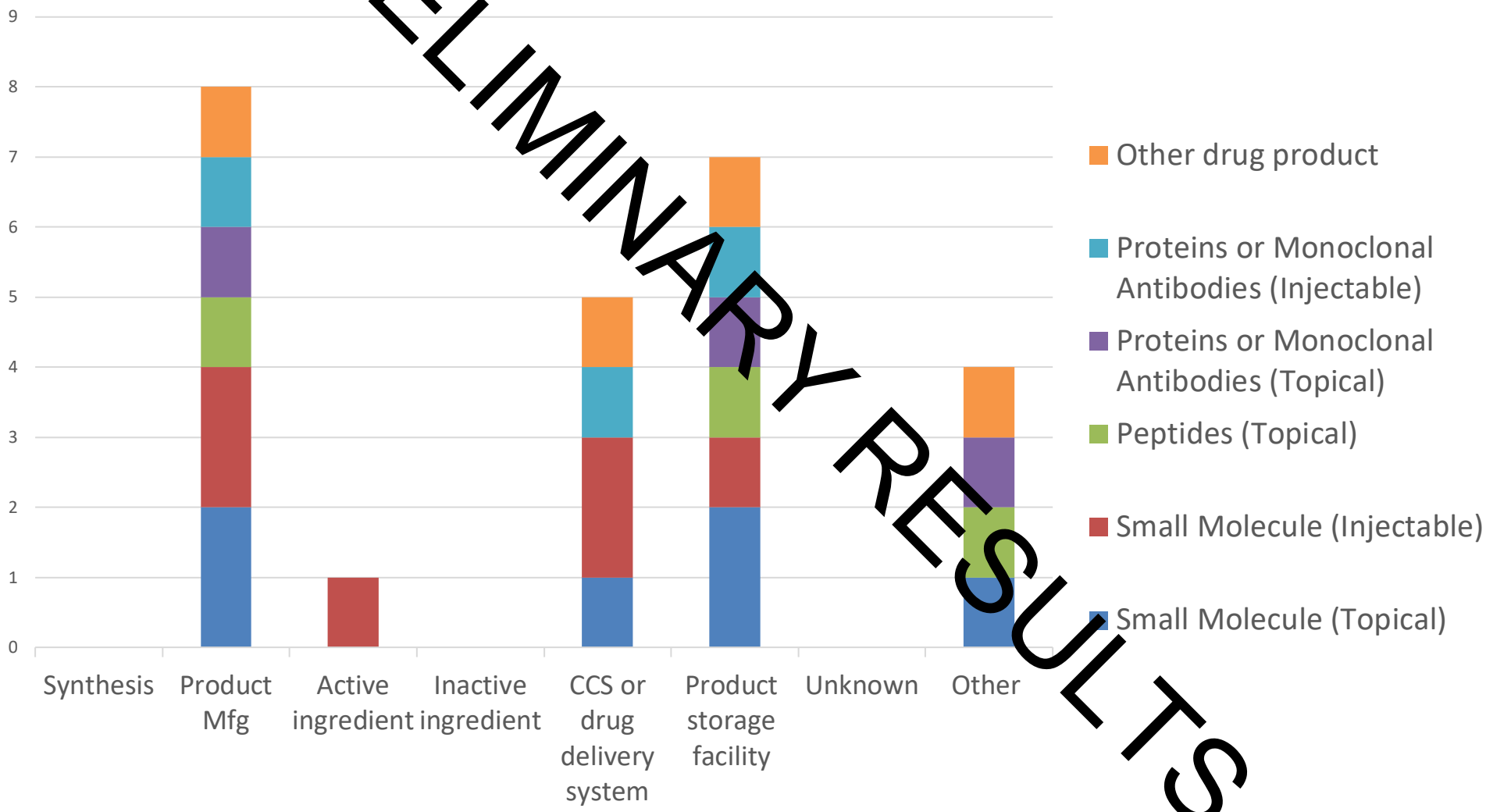
PRELIMINARY RESULTS



PHARMA Q:

Of the selected product types impacted by the proposed PFAS ban in Europe, how is PFAS used to make these products? Please select all that apply

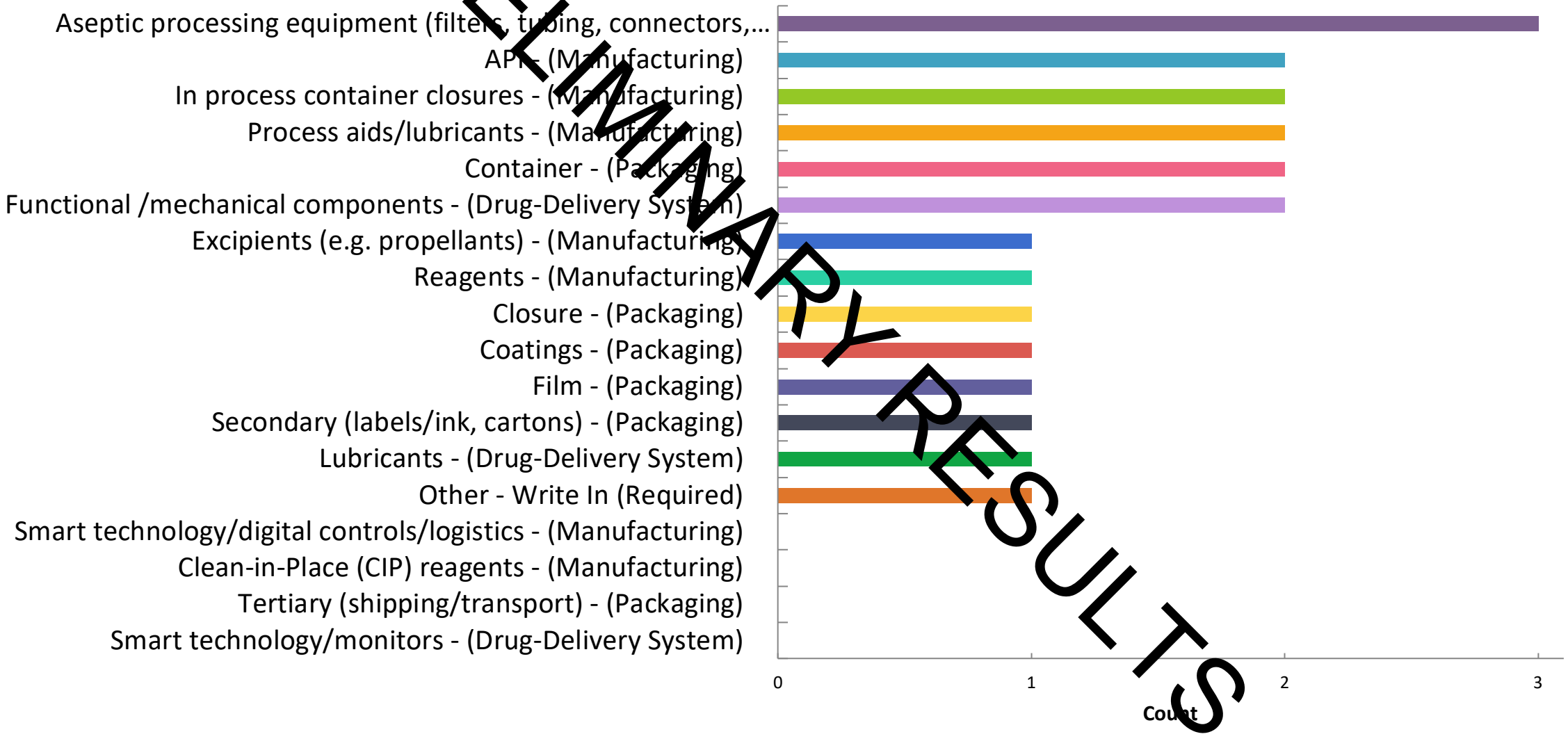
PRELIMINARY RESULTS



PHARMA Q:

Are you aware of any materials/components received from your company's suppliers that contain PFAS or would be impacted by the PFAS ban being proposed by ECHA? Please select all that apply.

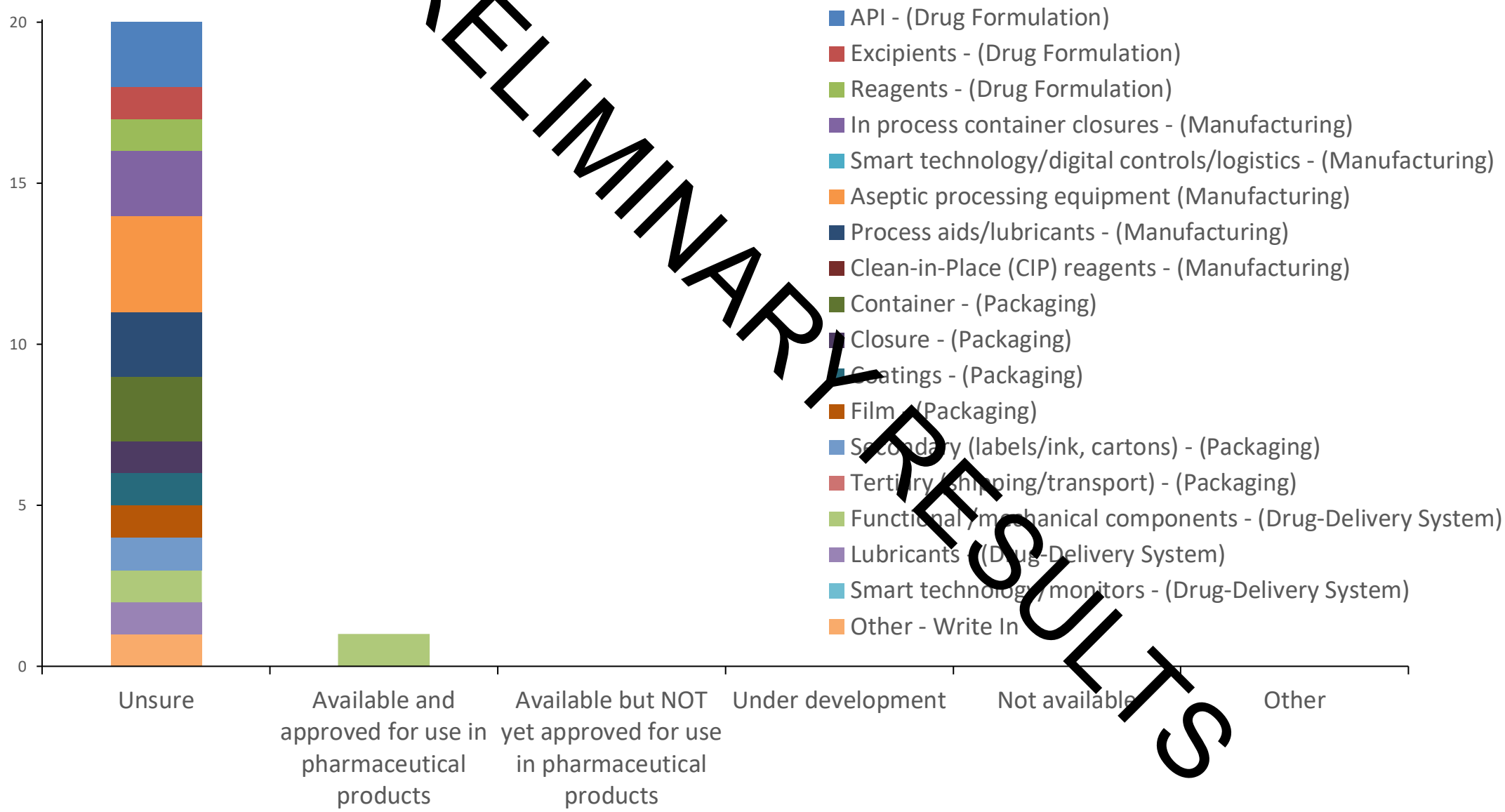
PRELIMINARY RESULTS



PHARMA Q:

Are you aware of the status of non-PFAS alternatives to the PFAS-containing material/component? Please select all that apply.

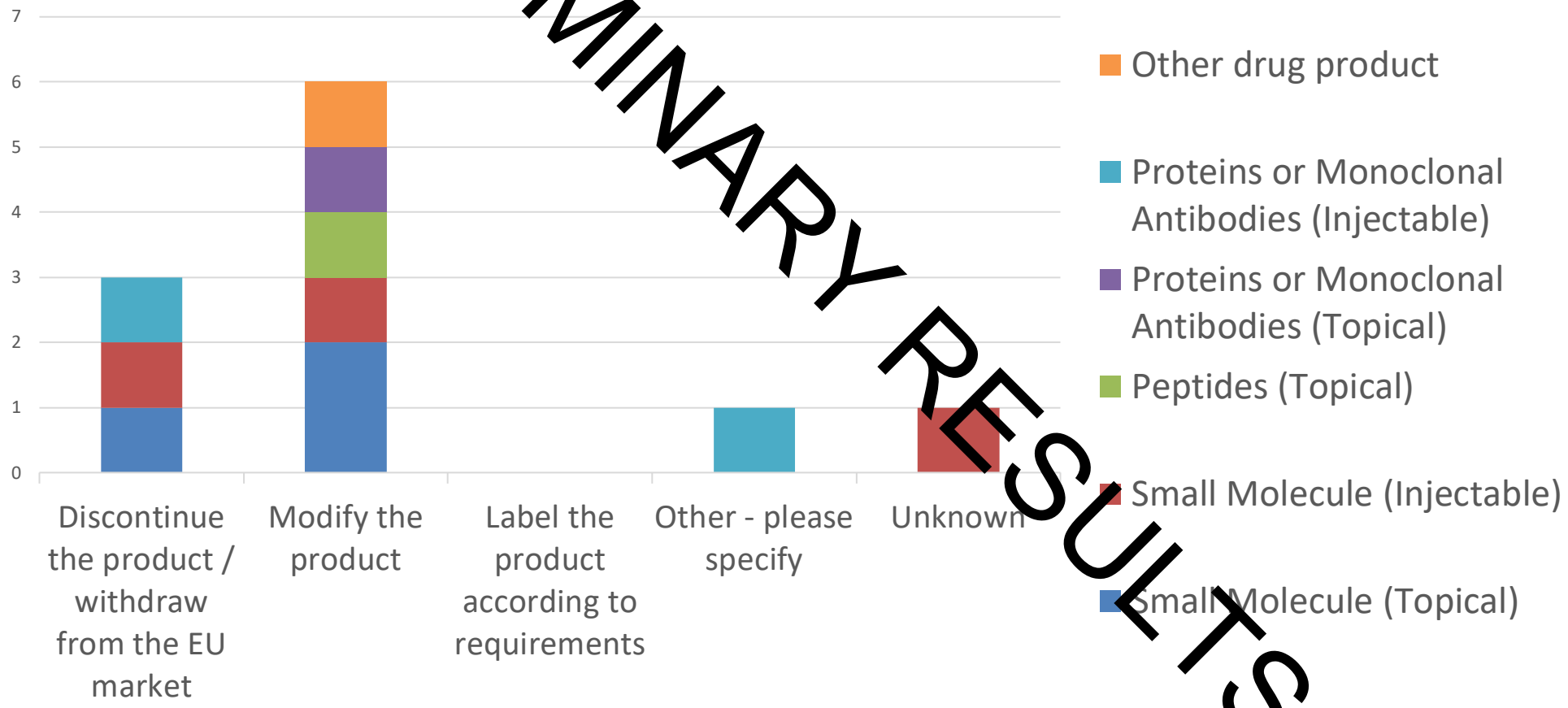
PRELIMINARY RESULTS



PHARMA Q:

Of those selected product types impacted by ECHA's proposed PFAS ban, if the PFAS material/component is used in your product, what would be the likely outcome when the ban takes effect? Please select all that apply.

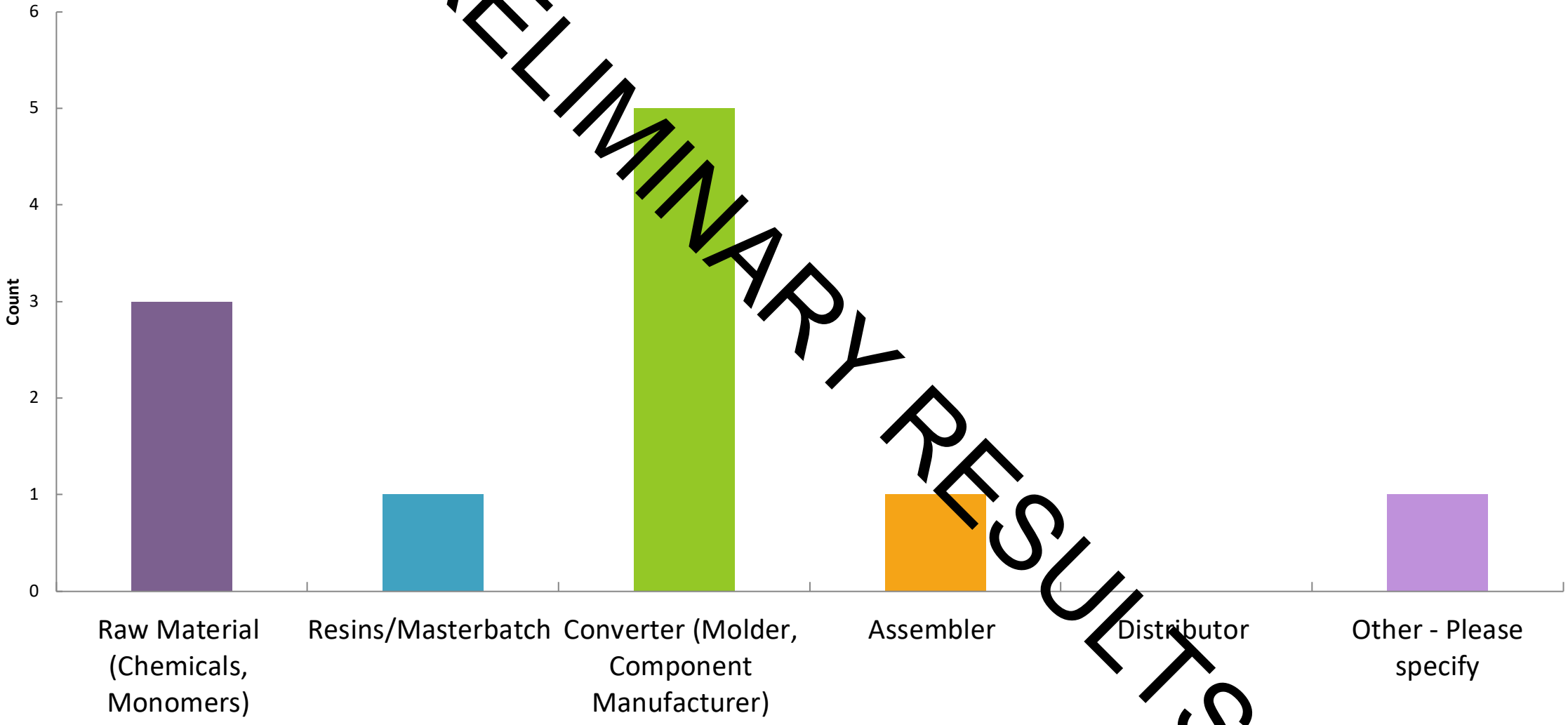
PRELIMINARY RESULTS



SUPPLIER Q:

Which of the following best describes the types of materials you supply? Please select all that apply.

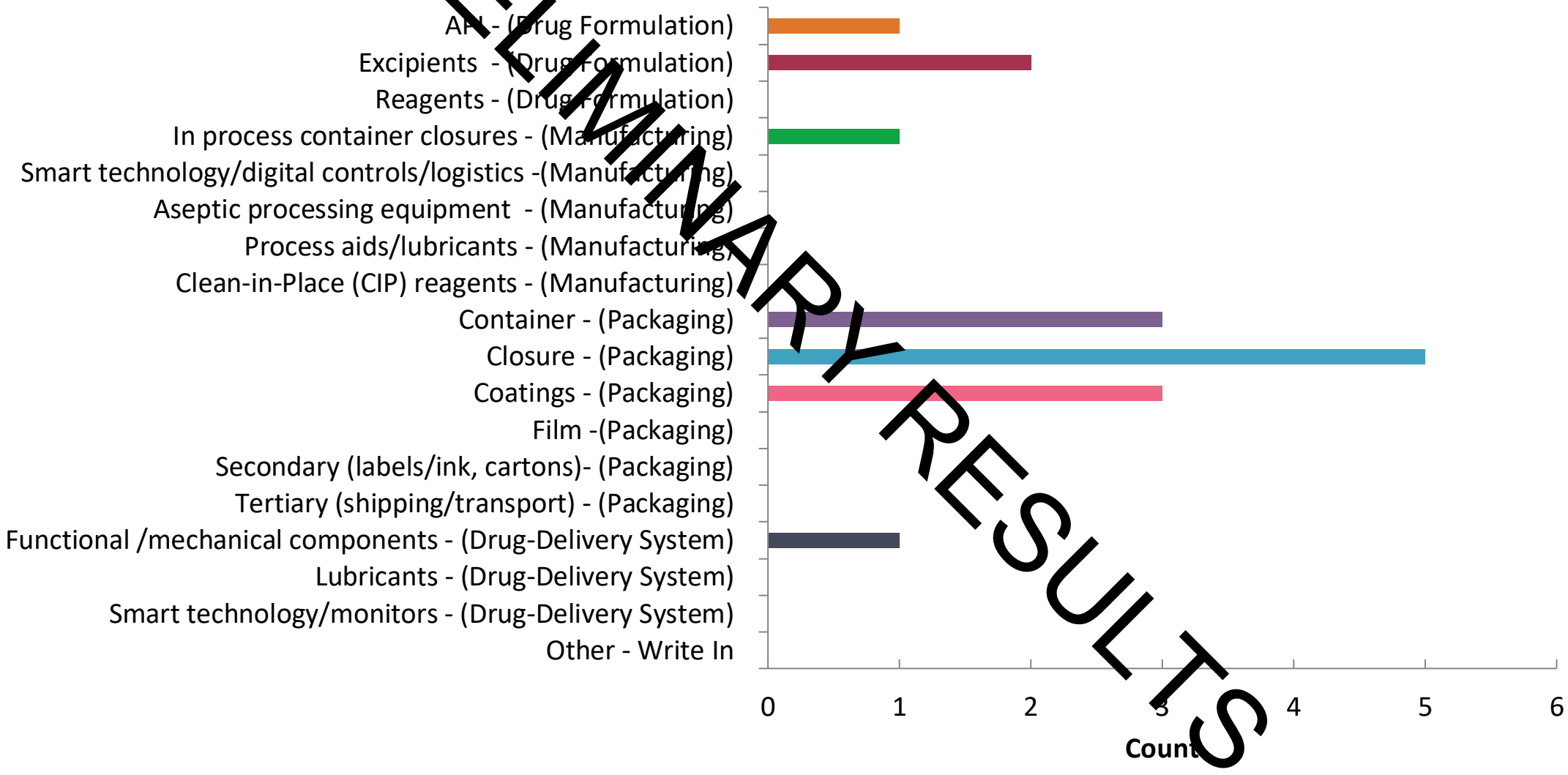
PRELIMINARY RESULTS



SUPPLIER Q:

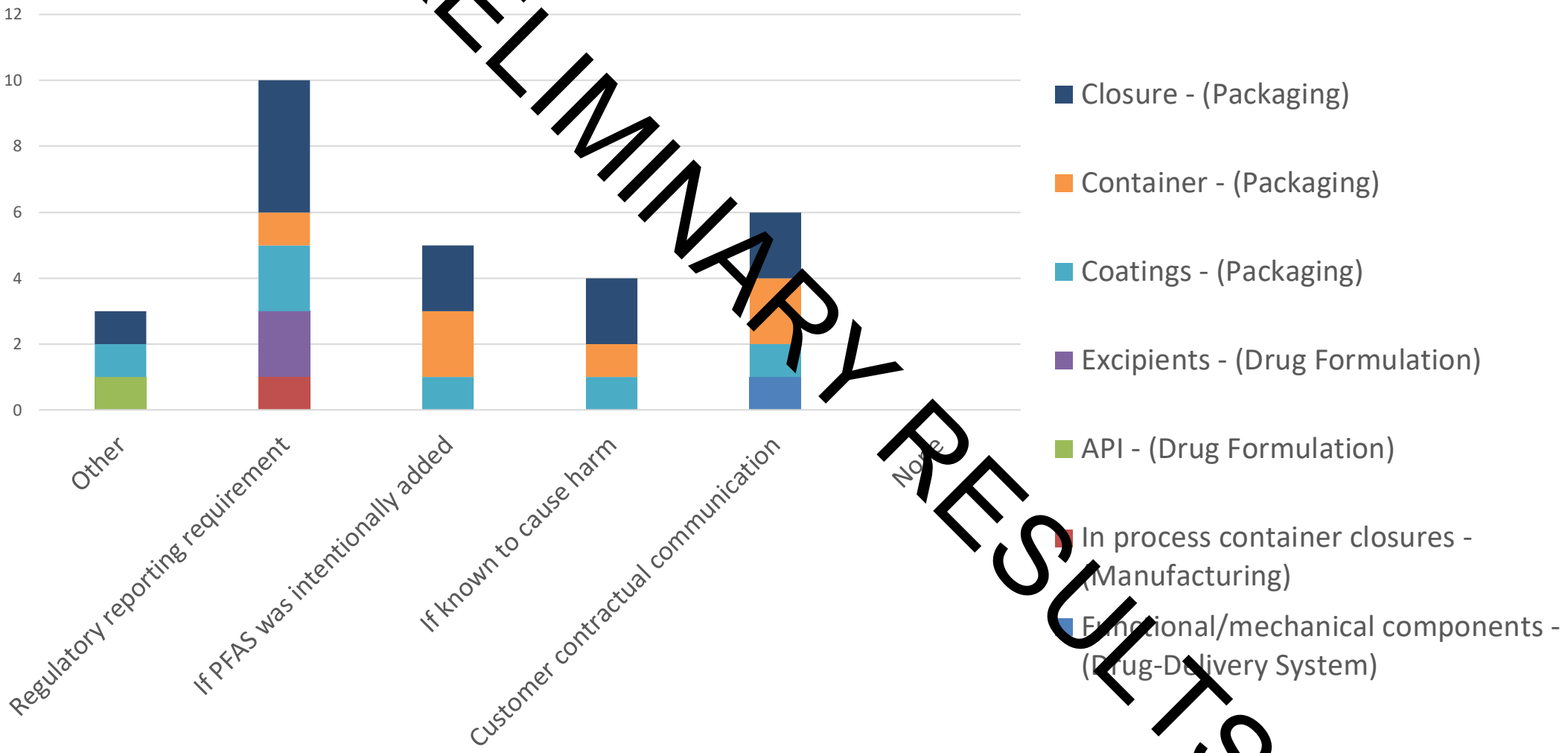
Of the materials that your organization supplies to pharmaceutical companies, which of the following types would be impacted by the PFAS ban being proposed by ECHA? Please select all that apply.

PRELIMINARY RESULTS



SUPPLIER Q

Under what conditions would a customer be notified if a product contains PFAS? Please select all that apply.



PRELIMINARY RESULTS

Questionnaire

- Reminder, please complete the questionnaire.
- Deadline – August 18, 2023
- Use this link http://s.alchemer.com/s3/PFAS-Survey
- Or use the QR code:

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Assessment of Impact of PFAS Ban and Planning Ahead Pharma Perspective

Presented by Atish Sen, AstraZenca

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Open Q&A

Diane Paskiet, West Pharmaceutical Services
Atish Sen, AstraZeneca
Quintin Lai, West Pharmaceutical Services
Cheryl Stults, C&M Technical Consulting, LLC
Helen Derbyshire, Kindeva
Rik Lostritto, Consultant

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Thank you for attending the webinar!

For more information on PQRI, visit our website at: www.pqri.org

Questions? Contact the PQRI Secretariat at: PQRISecretariat@pqri.org

Call for Volunteers

If you or your company is a member of a PQRI member organization (ELSIE, FDA, Health Canada, IPEC-Americas, IPAC-RS, PDA or USP) and you would like to participate in any of the PQRI Technical Committees, please contact the PQRI Secretariat (PQRISecretariat@pqri.org) for further information.

UPCOMING PQRI EVENTS:

- ***FDA/PQRI Workshop on the Regulatory Framework for the Utilization of Artificial Intelligence in Pharmaceutical Manufacturing*** – An Opportunity for Stakeholder Engagement - A Virtual Event on September 26-27, 2023
- ***PQRI Workshop: MIDD Approaches in Pediatric Formulation Development*** – A hybrid event on November 14 -15, 2023

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