Takeda's Approach to Navigating PFAS Challenges

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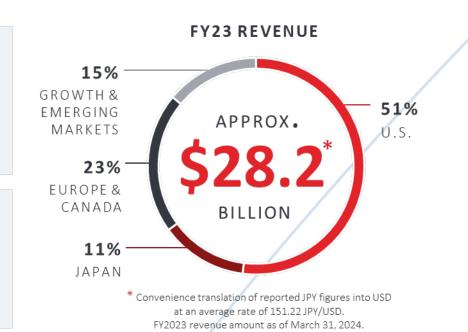
Takeda – a global biopharmaceutical company

TOKYO, JAPAN

CAMBRIDGE, MA, USA

~ 25 NEW MOLECULAR ENTITY CLINICAL STAGE ASSETS

COUNTRIES & REGIONS



1781

OSAKA, JAPAN

25+ MANUFACTURING SITES

2 RESEARCH SITES

180+
PARTNERSHIPS TO HELP
US BRING INNOVATION
TO PATIENTS

TOP EMPLOYER®
IN

24

COUNTRIES & 3 REGIONS



OUR PEOPLE

NUMBERS AS OF JUNE 2024
UNLESS OTHERWISE INDICATED

Agenda

- PFAS in Pharmaceutical Manufacturing
- Takeda's Risk Mitigation Strategy, Challenges and Digital Tools Created
- Key Takeaways



PFAS Overview: Role in Pharmaceutical Manufacturing



PFAS: per- and polyfluoroalkyl substances:

Substances that contain at least one fully fluorinated methyl (-CF3) or methylene (-CF2-) carbon atom (without any H/Cl/Br/l atom attached to it).

PFAS are widely utilized across our pharmaceutical development, manufacturing and supply in materials, reagents and kits due to their **inertness & hydrophobicity.**

More than 300 fluorinated compounds have been launched as drugs over the last few decades and today about 30% of all APIs contain fluorine.

PFAS are bio-accumulative **long-lasting chemicals**, components of which break down very slowly over time, posing risks to human health and the environment. Also known as **"forever chemicals"**.

Examples of widespread impact Distribution & Use R&D Manufacturing Laboratory Chemicals Production Packaging Storage & transport Application equipment Medical device. APIs. Stoppers, equipment Equipment, Starting materials, Blisters Plastics. Drug delivery Instruments, Pipes, Gaskets, Intermediates. Coatings. devices Caps, Valves, Pipina Process materials Refrigerants Injector, Degasser Filters, Refrigerants, Lubricants

European Federation of Pharmaceutical Industries and Associations. (2024, March 1). *PFAS* [Infographic]. EFPIA. https://www.efpia.eu/media/k24nszud/pfas-infographic.pdf



ECHA Proposed PFAS Ban & Takeda's Strategy





European Chemicals Agency
(ECHA) has proposed a ban on
over 10,000 PFAS substances
that find widespread use in
various industries and products.

Additional agencies/regions likely to enact regulations (reporting, bans, etc.).

Takeda initiated a strategic, centralized, cross-functional program to address and mitigate risks the proposed ban.

This is crucial for Takeda for several reasons:



PATIENT CARE AND SAFETY

Reliance on PFAS for safe manufacturing, distribution, and use of medicinal products underscores the importance of addressing potential disruptions in patient care.



REGULATORY COMPLIANCE AND REPUTATION

By engaging in a centralized cross-functional program to address the proposed ban, Takeda demonstrates its commitment to compliance with regulatory requirements and its responsibility to the environment and public health.



BUSINESS CONTINUITY

Potential business impact & disruption of Takeda's operations with ban on PFAS is significant, as highlighted by the tight timeline and reliance of the pharmaceutical industry on PFAS.



Takeda's Problem Statement and Plan



PROBLEM STATEMENT

No centralized repository of PFAS uses available.

The current draft regulatory proposal leaves many PFAS uses in the pharmaceutical manufacturing process in scope of restriction.

Final draft regulatory proposal TBD

TAKEDA INTERNAL PFAS TEAM

Assess scope of PFAS in relation to patient supply ahead of ECHA and other regulatory decisions.

- Global, centralized cross-functional program.
- Proactive data collection, aggregation and presentation in a searchable database/dashboard to provide the landscape of PFAS uses at Takeda. Including commercial and development products, supplier and internal surveys.
- Risk mitigation strategizing and prioritizing as a network and in response to regulatory decisions.

- Not limiting data collection to ECHA ban, but rather getting benchmarking of all Takeda PFAS use for other potential PFAS regulations.
- Leverage industry collaborations for benchmarking, support, further publications and comments (EFPIA, BPOG).
- Support responses to internal and external inquires and requests for data on PFAS.



Comprehensive PFAS Control Strategy



PROACTIVE

- Conduct Data Collection / Benchmark Takeda's Risk
- Create Network Dashboard
- Develop Risk-Based
 Mitigation Strategies
- Implement Risk-Based
 Mitigation Strategies

REACTIVE

- Monitor environmental regulation landscape
- Use dashboard to filter and prioritize in response to evolving legislation
- Track incoming Supplier
 Change Notifications

LIFE CYCLE MANAGEMENT

- Not a snapshot; implement means to continually add new information / data through SharePoint
- Evaluate incoming materials for PFAS
- Launch Alternates
 Workstream



Proactive: Data Collection

Complexity of Takeda's Network with 25+ Manufacturing Sites North/South America, Europe and Asia

Data Collection Scope:

Purchased parts & raw materials of commercial and pipeline programs

Testing and release of commercial and pipeline programs

Spare parts for equipment and utilities

Intermediates, DS and DP containing PFAS

CMO/CDMOs and equipment suppliers

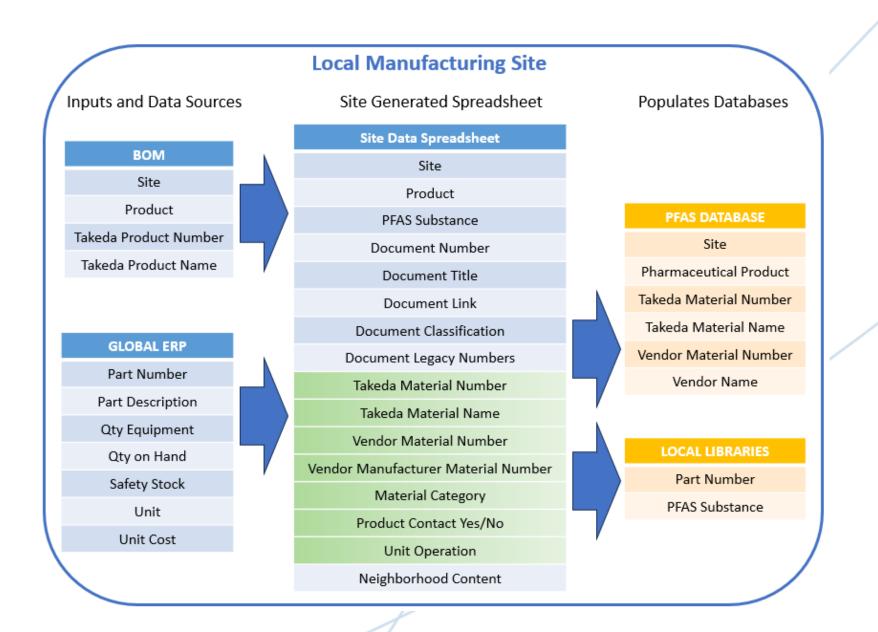


Proactive Data Collection: Localized Option



Problem Statement:

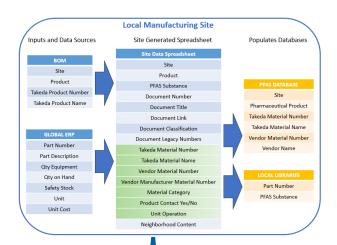
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Proactive Data Collection: Localized Option

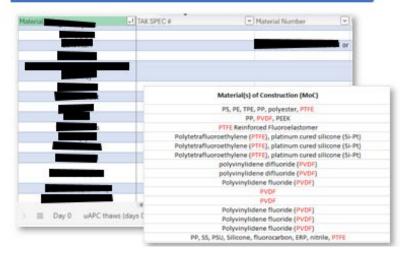




This process would be:

- Manual / labor-intensive
- Repetitive (at each site)
- Time consuming / inefficient







Grouping	Acronym	PEAS substance	Common name(s)/ Trade name (s)	RUPAC name	CAS number
Perfluoroaltyl acids	PHIS	Perfluorohexanesuffonic Acid	Lodyne Perfluorohexane sulfonabe Perfluorohexane 1-sulfonic acid	1,1,2,2,3,3,4,4,5,5,6,6,6- tridecaffuorofesane-1- suffonic acid	355-46-4
Perfluoroalityl acids	PHIA	Undecaffuorohexanoic acid	Perfluorohexanosc acid	2.2,3.3,4.4.5.5.6.6- undecaffuorohexancic acid	307-24-4
Ruoropolymen	PCTRE/PTRCE	Polychlorst-fluoroethylene	EIL-F* Neuflor* Policy chloro 1, 3, 2-trifluoroethylene) Chlorotrifluoroethylene polymer Tetrachtorohexafluorobutane	Ethene, 1-chloro-1,2,3-triffuo	9002-63-9
Fluoropolymens	ETHE	Ethylene tetrafluoroethylene	Tefon [®] ETFE Fluor [®] ETFE	Poly(1-pentene-2, 1, 1, 4, 4, 5, 5	15038-71-5
Fluoricarbonates	THE	fletrafluoroethylene	Dysecon** Fluors Fluors Enroter#F5-200 KT-1000A, KT-400M KT-450A, KTL-484, KTL-610,	1, 1, 2, 3 fetrafium certylene	116-14-3
PFAS	PFOS	Perfluorooctanesulfonic Acid	Fluorad	1,12,2,3,3,4,5,5,6,6,7,7,8	1763-23-1
Perfuorcalitylacids (PEAA)	PFBS	Perfluorobutanessifonic Acid	FC-98 Noneffate	1,1,2,1,1,1,4,4,4 Nonefuoro	175-71-5
Ruoropolymers.	PTPE	Polytetrafluorsethylene	Teffun" Chemfluor* Poly(tetrafluoroethylene)	Ethene, 1,1,2,2 netrafluoro-,	9002-88-0
PFAS	PHOA	Perfluorooctanos: Acid	C8 Fentadecaffuorsoctanoic acid	223344556677888	335-67-1
Rubropolymens	PVDF	Polyvinylidene fluoride	Solet" and Hylar"	Ethene, 1.1-diffuoro-, homop	24907-79-9



Product	Hodelity	Unit Operation (Dynamic Dropdown)	Material Category	PFAS Substance
TAK-188	ADC		22	
TAK-280	Biologics	127700000000000000000000000000000000000	I was	1 Jugaren Germann
TAK-188	ADC	Chromatography	Beg	Tetrafluoroethylene
MHTT SNP3 ASO	Oligonucleotides		J. 1755	
TAK-227	Synthetic_Molecules			
700				
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Proactive Data Collection: Initial Global Solution



Strategy to Minimize Site Efforts

All chemicals and SUTs

Too large of a scope, unnecessary data processing and review.

Common across sites: Global DDMS

Semi-automate PFAS identification from DDMS

Focusing on PFAS containing items. One global list. One time mapping of PFAS substances.

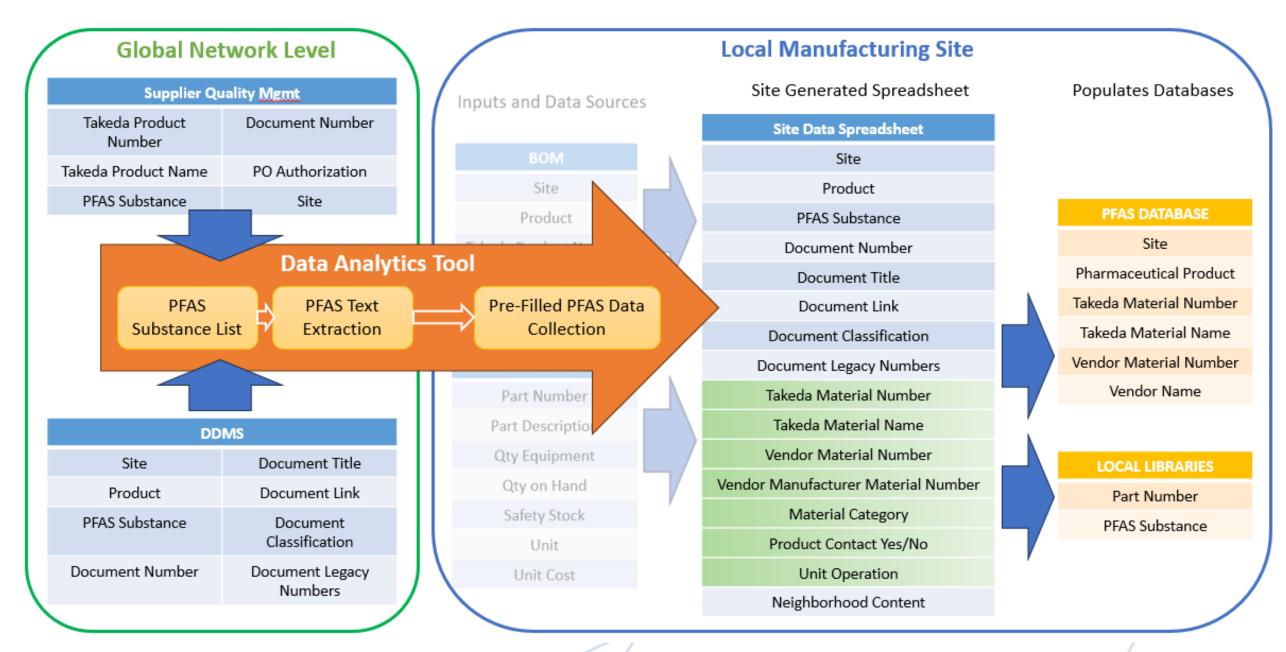
Filter by Sites

After piloting this approach: Still time consuming, slow interface and manual steps required.



Proactive Data Collection: Improved Global Solution







Data Aggregation into Searchable Dashboard



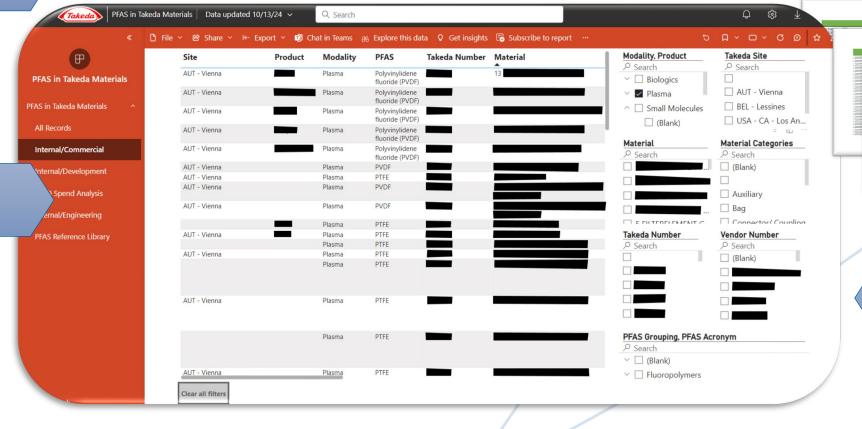




Surveys: Contract Lab, CMO, CMDO, Equipment Suppliers

satisfies an entire process of the control of the c

Dashboard



Internal Site Data: Eng'g Commercial, Pipeline, QC





Dashboard Utilization



PROACTIVE

- Develop Risk-Based Mitigation Strategies
- Implement Risk-Based Mitigation Strategies
- Visualization of risk

REACTIVE

 Use dashboard to filter and prioritize in response to evolving legislation

LIFE CYCLE **MANAGEMENT**

• Not a one-time data grab; implement means to continually add new information through SharePoint



Dashboard Utilization: Conceptual Demonstration



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Conceptual Demonstration:

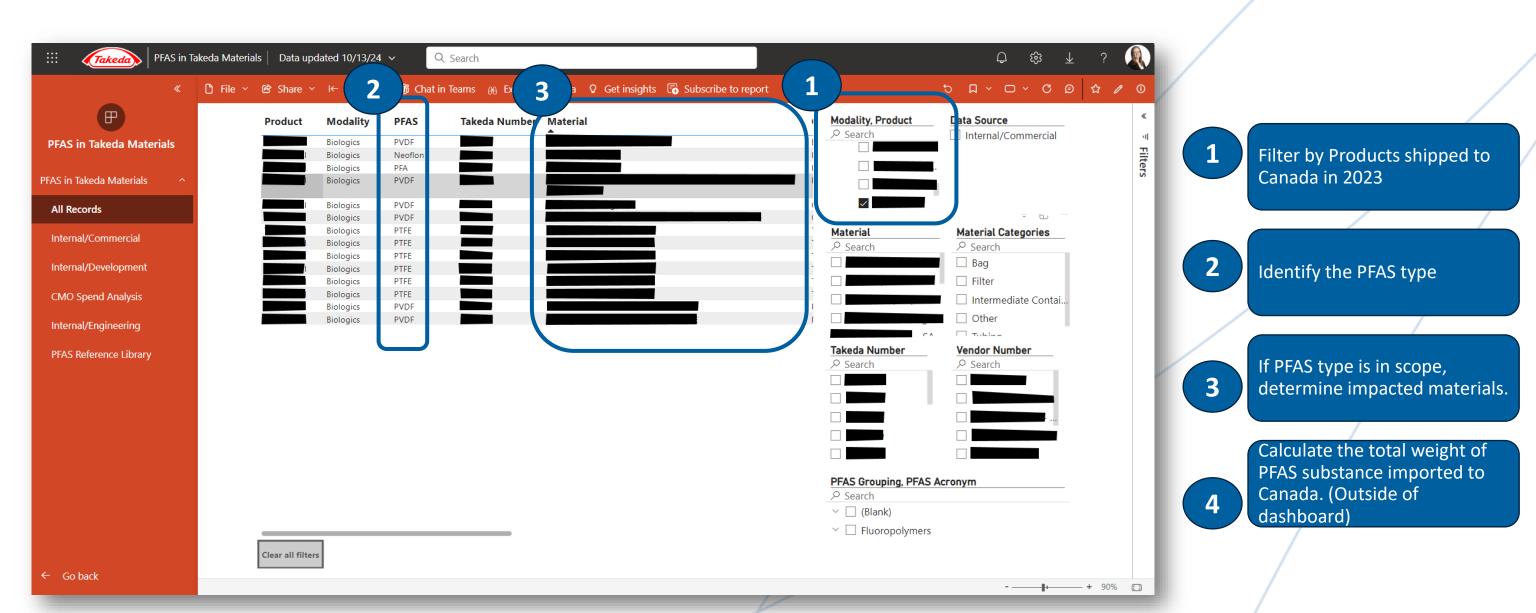
Reporting Requirement: Canadian Environmental Protection Agency (CEPA).

PFAS team could use the dashboard to identify items to be included in the report, those containing certain PFAS substances, distributed to Canadian region



Dashboard Utilization: Conceptual Demonstration







PFAS Key Takeaways



- The trend of emerging substances of concern in bio/pharmaceutical manufacturing is expected to continue.
- 2 Regional variations in legislation pose challenges for global corporations in assessing impact.
 - Takeda's structured approach leverages digital solutions and a master database to proactively prepare for future legislations and create a risk visualization roadmap in a complex, dynamic
- prepare for future legislations and create a risk visualization roadmap in a complex, dynamic environment.
- Future opportunities: Collect material metadata upfront in a central database, combining ERP and DMS information, to be ready for additional emerging substances of concern. Suppliers should identify substance of concern and align on data requirements.



Questions

