EUROPEAN FEDERATION OF CLINICAL CHEMISTRY
AND LABORATORY MEDICINE

Information sheet regarding REACH Regulation 1907/2006 on restrictions of Triton substance use in IVD reagents

Background

In July 2017, the substance **4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-OP) and 4-nonylphenol** was added to Annex XIV of Regulation (EC) No 1907/2006 ('REACH Regulation')[1] with a sunset date of January 4th, 2021. After this date, this substance can no longer be placed on the market or used in the EU unless subject to Authorisation (or exemption).

4-tert-OP and NPE are commonly used substances in the *in vitro* diagnostic (IVD) medical devices industry, where their primary function is to ensure the specificity and sensitivity of diagnostic tests for hundreds of different diseases and conditions. These diagnostic tests are specifically balanced and designed to perform biochemical reactions at the molecular level when combined with patient samples, and re-designing these tests with different substances is an extremely challenging and technical process subject to stringent regulatory requirements including testing, validation and country registrations which can take 5-12 years to complete per product.

As such, a number of IVD companies have applied for Authorisation on behalf of their EU customer base (Downstream Users) to ensure the undisrupted supply of diagnostic tests to the EU, while work is undertaken to phase out 4-tert-OP and NPE through extensive product re-development programmes. Please note, that an exemption in Article 56(3) of REACH known as the SR&D Exemption does apply to IVD downstream users, however there are conditions that must be adhered to and due to the lack of a full regulatory definition of "Controlled Conditions" many IVD companies chose to apply for Authorisation for the security of IVD supply in the EU.

Despite entering into the process of Authorisation in good faith, and making significant efforts and investments to re-design carefully balanced and stringently designed biochemical products, **the Draft Opinions prepared by the Risk Assessment Committee (RAC) & Socioeconomic Assessment Committee (SEAC) in regard to the majority of these applications now recommend that Downstream Users are subject to the following conditions:**

"All solid and liquid waste shall be collected for adequate treatment. The treatment shall minimize releases to environmental compartments as far as technically and practically possible. Release into the sewer system or to surface waters is not adequate treatment."

[1] Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)

Compliance with these conditions will put the supply of IVD products in the EU at risk, given the significant impacts associated with their implementation.

Technical Feasibility

At present, to comply with the wording of the RAC & SEAC conditions noted above **the only viable option for EU healthcare systems would be collection and incineration of wastewater as there is currently no known treatment technology proven to effectively remove dilute concentrations of 4-tert-OP and NPE from the wastewater generated from reagents used upon IVD instrument platforms.**

In addition, Downstream Users are already required to comply with the EU legal framework for wastewater management, where permission is sought from the water authority (or equivalent body) to discharge wastewater to sewer dependent upon the profile, and the conditions put forward would over-ride the existing legal requirement. The collection and incineration of wastewater for the EU healthcare system as a blanket approach across the board would be technically and practically infeasible at many locations, add disproportionate costs and disruptions to critical healthcare operations, and bring added emissions of CO_2 into the environment.

The volume of 4-tert-OP and NPE in the wastewater of most IVD instruments is extremely low, whereas the volume of wastewater itself can be extremely high. This is because of the wash cycles which must occur between every single test to clean the relevant parts of the instrument and ensure no cross-contamination of patient samples. Some instruments perform thousands of tests per hour. As a result, we estimate that millions of tonnes of wastewater will be generated and must be transported by road and incinerated each year, for the treatment of a minimal proportion of 4-tert-OP and NPE.

In addition, access to suitable incineration plants is problematic for downstream users in certain locations, with distances to suitable hazardous waste incineration plants varying from about 100 up to 1500 km. At these higher distances, and with trans-frontier waste shipment required in some cases, the transport would not be feasible.

Logistical Feasibility

There are also serious impracticalities in regard to the implementation of these conditions, these include

- The installation of new drainage networks in hospital and laboratory environments where civil works may need to be navigated through wards, clean rooms, etc.
- The installation of a dedicated collection system, which at hospital sites with large diagnostic laboratories would typically need to be an external tank system with bunding and secondary containment, and enough room for a tanker lorry to manoeuvre to make regular wastewater collections
- The lack of space generally experienced in healthcare settings, particularly in urbanised areas, will be a major issue in certain locations, both internally and externally
- The health & safety aspects, i.e. ergonomics, of transferring wastewater previously plumbed directly to drain, now being collected in the instrument waste container and transferred manually where applicable. Please note some high throughput systems produce >1 tonne of

wastewater/day and as such any manual transfer would simply not be feasible (the system design is not even set up for this)

The above also introduces a higher risk of overflow of wastewater within the clean laboratory testing environment

Economic Feasibility

As noted previously, the volume of 4-tert-OP and NPE in the wastewater of most IVD instruments is extremely low, whereas the volume of wastewater itself can be extremely high, as such the cost of wastewater collection and incineration will be extremely high. Costs of incineration are typically in the €1000/tonne range, and we estimate that over a million tonnes of wastewater will be generated in scope of these conditions.

Other costs to consider would be those required to install new drainage networks and tank systems for collection facilities at each location referred to in the previous section on 'Logistical Feasibility'.

Please also note that the costs above would be in addition to the significant investments already being made by IVD companies who have applied for Authorisation. These companies are making significant investments to their Substitution Plans to phase out 4-tert-OP and NPE in their product portfolios. These efforts are expected to reduce the volume of 4-tert-OP used and any subsequent release substantially.

While these Substitution Plans are underway, it would not make sense for EU healthcare institutions to allocate capital budgets to implement wastewater collection facilities and make incineration arrangements (where available) when the 4-tert-OP and NPE will be reduced and removed through the substitution efforts in parallel.

Societal Impact

The socio-economic impact of complying with these conditions is disproportionate, particularly when considering the significant efforts and investments already underway by the industry to phase out the substances.
The proposal puts at risk the availability and supply of medical technology products to healthcare institutions and patients across Europe. This will impact the ability to monitor and treat medical conditions and ensure safety of diagnostic testing in Europe and worldwide, thus impacting patient safety and public health, resulting in a negative impact on the public health system.

Please also note that laboratory tests in scope of these conditions include 'STAT' assays where results are required urgently within a matter of hours and can provide critical information that can affect the patient's treatment and is potentially life-saving. Examples include cardiac markers for diagnosis of myocardial infarction (heart attack), ßhCG (pregnancy), respiratory emergencies, shock and toxicological/poisoning emergencies. Any additional efforts or disruption caused by implementing additional wastewater collection arrangements pose a risk of causing delays.

Competitive Disadvantage

It is also of concern to us that conditions for use have not been applied equally across all downstream users. Conditions should be equitable and irrespective of different timelines for substitution plans and different volumes of 4-tert-OP and NPE covered in different applications. Requiring different conditions of use will create a competitive imbalance, given that all applicants' customers would not face the same economic burden.

Also, besides the potential competitive advantage for companies that have applied for Authorisation, some companies fall out of scope due to the exemption for mixtures below 0.1% substance concentration and the use of Annex XIV substances in scientific research and development (SR&D) under Article 56(3) of the EU REACH Regulation. In these circumstances, emissions of potentially much higher amounts will continue without obligations or requirements to reduce emissions.

Summary

As set out above, the proposed conditions are unrealistic and unfeasible for medical labs at this short notice due to technical, logistical and financial constraints. Also, the recommendation will introduce a competitive disadvantage for some applicants and downstream users. The proposed conditions, if implemented, are disproportionate and would pose a serious risk to the continued operation of testing laboratories and as such could result in severe delays in diagnosis and treatment for millions of EU patients. Potential risks to human health as a consequence of the proposed conditions of Authorisation must be given appropriate consideration.

IVD-manufacturers currently ask authorization to enable continuity of IVDs on the European market. If IVD-manufacturers get their authorizations for continued use of these detergents, the conditions for use required by REACH are deviated to the end-users.
The recommended REACH instructions to end-users are: ***"All solid and liquid waste shall be collected for adequate treatment. The treatment shall minimize releases to environmental compartments as far as technically and practically possible. Release into the sewer system or to surface waters is not adequate treatment."***

As there is currently no known treatment technology proven to effectively remove dilute concentrations of 4-tert-OP and NPE from the wastewater generated from reagents used upon IVD instrument platforms, this implies that **EU healthcare systems and diagnostic laboratories should collect and incinerate all their wastewater.**

What to do about this? So far, the ECHA scientific committees RAS & SEAC do not understand that their recommendation to end users, at a date that will be specified in the authorization decisions, is not realistic nor feasible, and even harmful for patient care. Therefore, the strategy chosen is to inform the ECHA committees on the disproportionate consequences of their recommendation. To that end, a short survey on the impact of this ECHA recommendation for medical labs has been developed. Assuming that a reasonable amount of information will be gathered from this mini-survey regarding the (non-)feasibility of this recommendation, it is anticipated that ECHA may listen to arguments from laboratory professionals.

Planning of the European Commission: Formal decisions regarding the ECHA authorization process and allowances of IVDs containing Triton-type detergents will be taken by mid-September 2020. *Therefore, the EFLM survey on waste management in healthcare settings (only 4 questions!) should preferentially be filled in immediately after reading the newsletter and/or at latest per 8 September 2020*. This very short notice should not prevent us from doing the mentioned survey timely.

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Note that the information above is mainly based on a position paper from Medtech Europe, d.d. 15 July 2020.