[redacted] (REACH)
DG Internal Market, Industry, Entrepreneurship and SMEs, European Commission
Avenue d'Auderghem, 45
1040 Bruxelles

By registered mail and e-mail :
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DG Environment
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**Object: PFOA ban – Request for derogation for IVD products**

Dear [redacted]
Dear [redacted]

We, DIAsource Immunoassays, are an IVD company located in Louvain-la-Neuve Belgium. We are developing, manufacturing, and selling worldwide (including Europe) in-vitro diagnostics products for the diagnosis and follow-up of multiple diseases.

We are writing to you in your capacity as [redacted] in charge of the REACH Regulation and the POP Regulation respectively, for the following reasons.

**1.** One of our products portfolio uses PFOA as a critical component to perform an accurate diagnosis of vitamin D deficiency (See Appendix 1 for more information on our products – what they are used for – how they are used – the use of PFOA in these products).

As you might know, vitamin D deficiency is an important public health concern that has emerged as a pandemic because low levels of vitamin D in the blood are a risk factor for several chronic disabling disorders, including rickets, osteoporosis, cardiovascular diseases and cancers. Moreover, it is the most undermined, underdiagnosed and undertreated nutritional deficiency. Worldwide, about 1 billion people are estimated to have insufficient levels of vitamin D. Up to 70% of the European population suffers from Vitamin D deficiency, with different situations across countries. An accurate diagnosis and monitoring of vitamin D deficiency is therefore a critical health concern nowadays.

**2.** By a regulation 2017/1000 of 13 June 2017, the European Commission has incorporated PFOA into Annex XVII of the REACH Regulation.

As a result, PFOA:

- shall not be manufactured, or placed on the market as a substance on its own from 4 July 2020; [redacted]

- shall not, from 4 July 2020, be used in the production of, or placed on the market (i) as a part of another substance, as a constituent, (ii) in a mixture or (iii) in an article, in a concentration equal to or above 25 ppb of PFOA including its salts or 1000 ppb of one or a combination of PFOA-related substances.

However, according to Article 67.1 of the REACH regulation, these restrictions shall not apply to the manufacture, placing on the market or use of a substance in scientific research and development (hereafter "***SR&D***").

According to ECHA's Q&A 1442 (of 3 October 2018), the use of an Annex XIV substance when it is required, on its own or in a mixture, as part of an in vitro diagnostic (IVD) method (e.g. in a reagent, calibrator, control material or kit) is considered as scientific research and development and is therefore exempt from authorisation requirements if this activity is carried out under controlled conditions and in a volume not exceeding one tonne per year per legal entity. This interpretation is also confirmed by ECHA's Q&A 585 (of 3 October 2018)[1].

The Guidance on Scientific Research and Development (SR&D) and Product and Process Orientated Research and Development (PPORD) of 11 December 2017 also states the following (on page 7):

> *"REACH defines scientific research and development (SR&D) as any scientific experimentation, analysis or chemical research carried out under controlled conditions in a volume less than 1 tonne per year (Article 3(23) of the REACH Regulation).*
> *Examples of SR&D may include any experimental research or analytical activities at a laboratory scale such as synthesis and testing of applications of chemicals, release tests, etc. as well as the use of the substance in monitoring and routine quality control or in vitro diagnostics at a laboratory scale under controlled conditions."*

Furthermore, point 3 (c) of entry 68 of Annex XVII of the REACH Regulation provides that points 1 and 2 of the same entry (which define the restrictions applying to PFOA) shall only apply from 4 July 2032 to "*medical devices other than implantable medical devices within the scope of Directive 93/42/EEC*". In this respect, please note that our products do not qualify as implantable medical devices covered by the above-mentioned directive.

**3.** On 7 November 2019, the European Commission proposed a delegated act to amend the EU POPs Regulation with regard to PFOA, as a follow-up of an agreement reached at international level by the Conference of the Parties to the Stockholm Convention.

This delegated regulation proposes to amend Annex I to the POPs Regulation by including PFOAs. The amendment shall apply from 4 July 2020 onwards.

According to Article 3 of the POPs Regulation, the production, placing on the market and use of substances listed in Annex I, whether on their own, in preparations or as constituents of articles, shall be prohibited. However, Article 3 of the same regulation states that Article 3 shall not apply in the case of "*a substance used for laboratory-scale research* [...]".

[1] Q&A 585 and 1442 concern, in fact, Article 56 § 3 of the REACH Regulation which provides for an exception (also relating to SR&D activities) to the obligation to obtain an authorization to use substances listed in Annex XIV. However, we note that in Q&A 1304 (of 2 June 2017) relating to Article 67 of the REACH Regulation, ECHA itself considers that "the same approach can be broadly considered as applicable" for the exceptions referred to in Article 56 and those listed in Article 67 of the REACH Regulation. Moreover, the concept of SR&D in these two articles is defined in the same way by Article 3(23) of the REACH Regulation. Therefore, the concept of SR&D has to be interpreted in the same way under Article 56 and Article 67 of the REACH Regulation.

[redacted]

The concept of laboratory-scale research is not defined by the POPs Regulation but should certainly be given a similar interpretation to the one given to the concept of research under the REACH Regulation.

**4.** The fact that our products are solely manufactured, distributed and used by professionals, and are therefore never exposed to the public population, reduces the risk of contamination of the public. Moreover, the quantities used by our company are very limited in comparison to the other uses of PFOA, namely less than 1.5kg per year. This very fact clearly justifies the exemption under the Reach and POPs Regulations.

**5.** In view of the above, **our company would like confirmation from your part, stating that**:

- With regard to the REACH Regulation:
  - our products benefit from the exemption provided for SR&D activities;
  - in any case, our products are medical devices covered by the exemption referred to in point 3 (c) of entry 68 of Annex XVII;

- With regard to the POPs Regulation:
  - our products benefit from the exemption provided for substances used for laboratory-scale research.

We would be grateful if you could get back to us on these points as soon as possible.

**6.** This being said, we understand the decision to restrict the manufacture, the placing on the market and the use of a product such as PFOA.

Although our products are exempt from the REACH and POPs Regulations, our company is committed to removing PFOA from our products as quickly as possible.

Our company is making every possible effort to find a credible alternative to PFOA and consequently have it validated and registered by the competent health authorities. Our R&D scientists, regulatory affairs specialists and production teams are working hard to achieve a breakthrough in the short and/or medium term.

Given the importance of our products to public health, you will understand that, in the meantime, our company cannot stop the provision of Vitamin D assays for the diagnosis and monitoring of Vitamin D deficiency across the population. Last year, DIAsource Immunoassays has supplied hundreds of hospitals and clinical laboratories[2], for a total number of 1.825 million vitamin D tests. Moreover, Vitamin D assays are poorly standardized, which means that these hospitals and clinical laboratories cannot easily switch from our assays, to other assays available on the market. This requires a long and extensive validation process, especially keeping in mind the follow-up of patients, which can take up several years. Therefore, the sudden interruption in the provision of our products to the clinical community would have a major impact on the public health with the impossibility to diagnose vitamin D deficiency across a large number of patients, and with the interruption of the monitoring of patients that benefit from a treatment following an initial diagnosis performed with our products.

[2] Exact numbers are hard to collect as we supply a large part of our products to distributors, which themselves supply the hospitals and clinical laboratories.

[redacted]

Such sudden interruption would be avoided in the case where DIAsource Immunoassays is allowed to continue its supply of PFOA-containing Vitamin D assays while working on the development and validation of assays that do not contain PFOA.

**7.** We sincerely thank you for your attention to this letter. We are of course at your disposal for any further information you may require.

A copy of this letter is addressed to the European Chemicals Agency.

Furthermore, we are available to meet you if you wish, if necessary by conference call (for example through Skype or any other means of online communication...).

Sincerely yours,

[redacted]

DIASOURCE ImmunoAssays S.A.
Rue du Bosquet, 2
B-1348 LOUVAIN-LA-NEUVE (BELGIUM)
RPM T.V.A. BE 0457 934 723

Appendix 1

DIAsource immunoassays is a manufacturer of in-vitro diagnostic products (IVDs). These products are used by private and hospital clinical laboratories to analyse blood samples from patients, in order to quantify a number of hormones or proteins. The results of these analyses are used by clinicians to diagnose and monitor certain diseases, and take actions accordingly towards the patients.

The products concerned by the ban on PFOA are dedicated to the analysis of vitamin D in blood samples, in order to evaluate and monitor vitamin D deficiency in patients[3].

As explained above, vitamin D deficiency is an important public health problem that has emerged as a pandemic because low levels of vitamin D in the blood is a risk factor for several chronic disabling disorders, including rickets, osteoporosis, cardiovascular diseases and cancers. Moreover, it is the most undermined, underdiagnosed and undertreated nutritional deficiency. Worldwide, about 1 billion people have been estimated to have insufficient levels of vitamin D. Up to 70% of the European population suffers from Vitamin D deficiency, with different situations across countries. An accurate diagnosis and monitoring of vitamin D deficiency is therefore a critical health concern nowadays. Our products meet these needs by providing a reliable solution to the clinical community.

PFOA, in these products, has a critical role in allowing the quantification of vitamin D from the blood sample. It acts as a kind of sample treatment. Removing PFOA from the products simply prevents the measurement of vitamin D in these samples. The role of PFOA in our products is very different from the classical use of PFOA as a surfactant for many industries.

[3] See below an extract of the insert of two of the products concerned by PFOA. The complete versions and portfolio of products can be found on our website: https://www.diasource-diagnostics.com/IVD-Products/ImmunoAssays/Bone-Metabolism/Vitamin-D.

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**US: For in-vitro diagnostic use only.**

Read entire protocol before use.

# 25OH Vitamin D Total ELISA

## *I INTENDED USE*

Immunoenzymatic assay for the *in vitro* quantitative measurement of 25-hydroxyvitamin D2 and D3 (25OH-D2 and 25OH-D3) in serum.

## *II GENERAL INFORMATION*

A. **Proprietary name :** DIAsource 25OH Vitamin D Total ELISA Kit

B. **Catalog number :** KAP1971 : 96 tests

C. **Manufactured by :** DIAsource ImmunoAssays S.A.
Rue du Bosquet, 2 B-1348 Louvain-la Neuve, Belgium

**For technical assistance or ordering information contact :**
**Tel :** +32 (0)10 84 99 11 **Fax :** +32 (0)10 84 99 90

## *III CLINICAL BACKGROUND*

Vitamin D is the generic term used to designate Vitamin D2 or ergocalciferol and Vitamin D3 or cholecalciferol.
Humans naturally produce Vitamin D3 when the skin is exposed to ultraviolet rays.
In the liver mainly, Vitamin D3 is metabolised into 25-Hydroxyvitamin D3 (25OH D3) which is the main form of Vitamin D circulating in the body.
25OH D3 is a precursor for other Vitamin D metabolites and has also a limited activity by itself.
The most active derivative is 1,25-hydroxyvitamin D3, produced in the kidney (or placenta) by 1-hydroxylation of 25OH D3.
25OH Vitamin D stimulates the intestinal absorption of both calcium and phosphorus and also bone resorption and remodelisation.
25OH Vitamin D might also be active in other tissues responsible for calcium transport (placenta, kidney, mammary gland ...) and endocrine gland (parathyroid glands, beta cells...).
Vitamin D3 and Vitamin D2 are also available by intestinal through food or dietary supplementation.
As Vitamin D2 is metabolised in a similar way to Vitamin D3, both contribute to the overall Vitamin D status of an individual.
It is the reason why it is very important to measure both forms of 25OH Vitamin D equally for a correct diagnosis of Vitamin D deficiency, insufficiency or intoxication.
Vitamin D deficiency is an important risk factor for rickets, osteomalacia, senile osteoporosis, cancer and pregnancy outcomes.
The measurement of both 25OH Vitamin D forms is also required to determine the cause of abnormal serum calcium concentrations in patients.
Vitamin D intoxication has been shown to cause kidney and tissue damages.

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Read entire protocol before use

# 25OH Vitamin D total -RIA-CT

## I INTENDED USE

Radioimmunoassay for the *in vitro* quantitative measurement of 25-hydroxyvitamin D3 and D2 (25-OH-D3 and 25 OH-D2 ) in serum.

## II GENERAL INFORMATION

A. **Proprietary name :** DIAsource 25OH Vitamin D total -RIA-CT Kit

B. **Catalog number :** KIP 1971 : 96 tests
KIP 1974 : 4 x 96 tests

C. **Manufactured by :** DIAsource ImmunoAssays S.A.

Rue du Bosquet 2 , 1348 Louvain-La-Neuve , Belgium

**For technical assistance or ordering information contact :**
**Tel : +32 (0) 10 84 99 40 Fax : +32 (0) 10 84 99 90**

## III CLINICAL BACKGROUND

Vitamin D is the generic term used to designate Vitamin D3 or cholecalciferol and Vitamin D2 or ergocalciferol.
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The most active derivative is 1,25-Dihydroxyvitamin D3, produced in the kidney (or placenta) by 1 $\alpha$ - hydroxylation of 25OHD3.
25OHVitamin D stimulates the intestinal absorption of both calcium and phosphorus and also bone resorption and mineralization.
25OH Vitamin D might also be active in other tissues responsible for calcium transport (placenta, kidney, mammary gland...) and endocrine gland (parathyroid glands, beta cells...).

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The measurement of both 25 OH Vitamin D forms is also required to determine the cause of abnormal serum calcium concentrations in patients.
Vitamin D intoxication has been shown to cause kidney and tissue damages.

[redacted]