NEWSLETTER JUNE-JULY 2018

CHEMSAFE _ Here we are!!

The June-July edition of our Newsletter will be mainly focused on Chemsafe's activities and news regarding important targets reached and new activities implemented. As already said also on these Newsletter papers, 2018 is a crucial and very important year for our company. Since mid 2017, Chemsafe worked very hard to reach market positions in news fields in a period where the Business Unit "Chemical" staff was deeply involved on the 2018 Reach deadline. Therefore the efforts was double folded: on one side to keep all engagements due to Reach deadline and on the other side to keep the development of new activities strictly on line with our intentions.

Quality system 9001-2015 acquisition.

In late 2016, the "old idea" of our management to get the quality system certification became reality. The company decided to start all necessary actions to prepare itsself to be audited for such certification. We recruited a new person, "our quality person", who has been addressed to this target and we carefully selected an external consultant to support the activity of our quality person. The work to be done soon appears particularly challenging as it was not easy to standardized some/many of our activities which are purely scientific works where interpretation of results/studies and following discussion with the customers are basic elements. The creation of the documental parts (activities description, actions flows, reporting models and so on) involved all the staff of the three Business Units, the Management and the Business Development people. Hundreds of hours were spent for the creation of such documents. The final outcomes is represented by a documental archive of more the 250 papers. We got the first visit from the auditor on May 24 and the following two days on June 14-15. The auditor decided to inspect selected activities for the Pharma and Biocide/Agro Business Unit. The outcome of the inspection was very positive with only some minor suggestions. Some days ago we received the herewith certification from the certification company (Italian language only for the moment).

BUREAU VERITAS
Certification

CHEMSAFE SRL

Sede Legale:
Via Ribes, 5 – 10010 COLLERETTO GIACOSA (TO)
Sede Operativa:
Via Lugnacco, 4 – 10010 PARELLA (TO)

Bureau Veritas Italia spa certifica che il sistema di gestione dell'organizzazione sopra indicata è stato valutato e giudicato conforme ai requisiti della norma di sistema di gestione seguente

Norma

ISO 9001:2015

Campo di applicazione

Consulenze tecnico-regolatorie nel settore della chimica, farmaceutica e cosmetica.

Settore/i EA di attività: 34

Data d'inizio del presente ciclo di certificazione: 09 luglio 2018

Soggetto al continuo e soddisfacente mantenimento del sistema di gestione questo certificato è valido fino al: 08 luglio 2021

Data della certificazione originale: 09 luglio 2018

Certificato N. IT282045 Rev. N. 1 del: 09 luglio 2018

ANDREA FILIPPI - Local Technical Manager

Indirizzo dell'organismo di certificazione:
Bureau Veritas Italia SpA Viale Monza, 347 - 20126 Milano, Italia

ACCREDIA

We are very proud of this success for many reasons!
Getting a quality certification is a confirmation that our scientific and regulatory activity is at utmost level. The certification includes chemical, pharmaceutical and cosmetic fields which are our historical core business; next steps will included also other sectors which are not yet covered. We will plan to implement the quality system in other fields the next year. Technical and Regulatory consultancy is included in the certification statement. The improvement plan of our quality system includes the creation of a centralized and secure archive of all the information/data/studies collected form data banks search and/or provided by our customers. This is a very critical point for the storage and confidentiality of data which are the core of our toxicological evaluations. The acquisition of a quality system is not common for a Regulatory Affairs company like us; we believe, especially for pharmaceutical/medical devices companies, that this will be a plus for us in the competition arena.

All people in Chemsafe contributed significantly to the successful acquisition of the quality system! ***Let me express to all of them our thanks and acknowledgments for the hard work done and, in particular, for having shared the passion and the meaning that this acquisition has for Chemsafe.***

New Business Unit: Medical devices

Chemsafe started operating in the field of Medical Devices two years ago following some "spot" request from occasional customers. The incoming new Regulation EU/2017/745 replacing the old Council Directive 93/42/EEC on Medical Devices and the sister Reg. EU 2017/746 for "in vitro Diagnostic" gave us a "*good reason*" to decide to invest in such new field of activities. We got a Biomedical Engineer and together with one of our biotechnologist (medical expertise) we created a small group belonging to our Pharma BU. In July this year, due to increase of expertise and, at the same time, increase in inquiries from customers, after the acquisition of the quality system, we formally create the forth Chemsafe Business Unit: the Medical Device one as an independent BU. Nowadays the Medical Devices Unit staff is composed by three people; a Biotechnologist with medical expertise acting as the Head of the BU, a Biomedical Engineer and a Quality expert.

We believe that Chemsafe MD BU, together with cooperation with the other BUs with and integrated approach, can support companies for many needs. In particular, due to our huge experience in data search and evaluation, we are very confident to be able to help companies with the clinical and safety evaluation of their products. Within our Pharma BU, but not only, well experience toxicologists (at least three) are available to guide the selection of the safety test as for the last guideline. Capacity to coordinate, by study monitoring, external safety and clinical studies as well as to prepare the complete technical dossier conclude our expertise in such area.

In summary activities offered are the following:

- *product classification (MD class definition)*
- *borderline products evaluation (combination products, pharmaceuticals, cosmetics, biocides, food supplements)*
- *Quality management system*
- *Review and evaluation of Technical documentation/design dossier*
- *Support on the conduct of biological evaluation within a risk management process*
- *Toxicological evaluation of DM materials*
- *Clinical evaluation report and plan*
- *Product submission to regulatory agencies*
- *Interaction with notified bodies and /or competent authorities*
- *"on site" training if requested to selected customers*

Business Unit Agro/Biocides: a trend to increase international presence

Chemsafe started its activity in the Agro/Bioicides area in 2010. From that time a constant growth of the work done in such a unit occured mainly in the biocides field with good opportunities in the agro too. We have presented around 100 dossier for different PTs in different EU countries. The BU is now a 4 experts staff distributed in the two area of interest (Biocidal Products and Agrochemicals). In late 2017 we decided to focus the Business Developmental Activity of this BU by the acquisition of a BD Manager. His target was/is to develop such activity in Italy and at international level. We started, therefore, attending important conferences/events both as exhibitors and speakers. The last TSGE conference in Prague (*Focus on SMEs - Keeping up with the progress on active substance approvals)* saw the participation of Francesca Fasano (BU Head) and Antonio Conto (Chemsafe Managing Director) with two interesting talks (respectively *Biocide by-products evaluation* and *Dossier management for SME*) with an interesting final discussion on some open matters with the audience. Next talks will be at Vienna event on Biocides (by Francesca Fasano) regarding *"in situ" biocides* and at an event in Poland (by Antonio Conto) regarding ***EDS*** (Endocrine Disrupting Substances) in autumn.

The Endocrine Disrupting Chemicals, in brief EDC, is a wide family of substances, indeed not yet well defined, that may induce harmful effects to the organisms (human and/or animals) acting through an interference action within the hormonal system. Since mid '90s, the Scientific Community have been started the discussion on how to define and characterize the EDC activity and some Regulatory Bodies in USA as well as in Europe started to build up draft positive lists. From those years up to now such a discussion was kept alive by the debate between regulatory bodies and chemical/pharmaceutical industry; in 2006 the EDC substances have been mentioned in the REACH Regulation (EC 1907/2006) within the group of the Substance of Very High Concern (SVHC). Recently the EDC category was also discussed within the regulations concerning Agrochemical and Biocides active substances and product in the frame of the cut-off criteria leading in some cases to additional special regulation publication. Regarding the pharmaceutical area, the assessment of a potential ED properties can heavily affect the ERA (Environmental Risk Assessment) of

medicine when placed to the EU market firstly. This paper aims to summarize up the approaches to identify ED (Endocrine Disruption properties) and EAS (Endocrine Active Substances) and will update about the recent EU specific regulation.
All of us surely share the ethical approach to protect the human health and the environment from ED chemicals so adversely and so sneaky in their action but industry is also concern about a possible disproportionate request from regulators which may lead to test a huge number of chemicals. Expenses to do so will create an unacceptable economic burden for industry; only large organization may bear it and, again, SME will be discriminated. Last but not least, both industry and regulators have to increase their assessment capacity hiring toxicologists that will need to have a broad knowledge including health regulatory toxicology, eco-toxicology, environmental fate processes, environmental biodegradation processes, secondary dietary risk assessment, specific adverse effects and so on in a frame of a more and more multidisciplinary and integrated approach.

Coming back to biocide products, in March 2018 we also created the task force on *Sodium Hypochlorite* putting together a panel of international companies. The task force is created on the basis of Reach principles where companies share the common "father" dossier and the complete testing set down on the basis of the meta evaluation of the family. Each of the members will then submit its own dossier. No same biocide product submission is foreseen in this business model. We are now building up other two Task Forces expected to start by the end of 2018.

Business Unit Chemical

The Newsletter of May 2018 ended with …..**REACH *is not finished.. we are only at the beginning!!***
Our Business Unit Chemical was subjected to a massime pressure to respect the deadline for a huge number of substances. Last 2018 six months period went crazy! But at the end we got our target! Chemsafe has successfully submitted more that 300 dossier by the deadline including "light registration" procedures for intermediate substances as well as Joint Submissions. This number lead to a total up to 800 of dossiers delivered in total since the beginning. An huge job!!
As you all know, ECHA informed that is still possible to submit registration of pre-registered substances (phase-in) for a certain period given that the production of importation of the related substances is stopped up to the registration number acquisition. There is lot of uncertainty regarding the validity period of this "possibility"; some claimed up to the end of 2018 some others… up to the end of May 2019 (just one year from 2018 deadline). ECHA will clarify this later.
Reach is not yet finished? It's true….. the regulation will continue to be applied for new chemicals (non phase-in substances) and for all the authorization/restriction procedures coming for the implementation of the candidate list and from dossier (Annex XV) submitted by Member States. Much work will be requested later to the formal evaluation of the registration dossiers submitted in 2018 mainly due to studies (type and number) implementation, risk assessment refinement for exposure scenario and application of exposure scenarios by downstream users.

Our BU Chemical is not only involved in the Registration activity but, through the work of its two subunits (SDS preparation and CLP classification) deeply supporting companies for the SDS review and new preparation and CLP classification (including transport and USA OSHA models). A particular need is related to the translation of SDS in the foreseen EU languages and even non EU in some cases.

CLP
Poison Centers Notification Format

We'd like to address your attention to the **PCN activity** in relation to the harmonization of the classification information of hazardous mixtures to be submitted to Member States Poisons Centers as for Art. 45 of the CLP Regulation. What follows is an extract of the ECHA web page regarding the PCNF.

The Poison Centers Notification (PCN) format structures the information on hazardous mixtures classified for health or physical hazards. This information has to be submitted to the Member States appointed bodies. The format is XML based and defined by the requirements laid out in Annex VIII to the CLP Regulation.

The information to be submitted includes the full chemical composition, toxicological information, relevant product and mixture details including the intended use (EuPCS), in addition to the label elements such as the Unique Formula Identifier (UFI). The PCN format aims to harmonize and ensure consistency of the information available to Poison Centers in cases of poisoning incidents in the EU.

Version 1 of the PCN format is compatible with IUCLID, a tool developed at OECD level, which promotes the harmonization of chemicals data and is available at the link below.

Note that version one of the PCN format may undergo further adjustments as a result of:
- *PCN format 'pilot project' run by ECHA in conjunction with stakeholders*
- *Any regulatory changes following a workability study contracted by the Commission.*

Any updates of the PCN format will be synchronized with the yearly IUCLID format update, published in October.

Download

To help with the IT implementation of this format, the following is available:

- PCN format (version 1.0, published on 30 April 2018): the format is made available as a set of XML scheme definition files (XSDs). There is also a data model that shows all relevant fields and their interconnections.
  Download the PCN format (53 KB | .zip)
  Download the PCN data model (533 KB | .pdf)

Part A - Preparing a PCN dossier: this document provides a technical background and offers a practical guide to the industry on how to encode, prepare and complete a dossier compliant with the PCN format. The XML content and the inner structure of the PCN format is explained in a simple manner avoiding technical details or jargons.
Download Part A – Preparing a PCN dossier (.pdf)

Part B - Developers' guide to the IUCLID format: in IUCLID, the exchange of chemical information is facilitated via a zip/archive file with the extension .i6z (IUCLID 6 zip). The information can be exported from one IUCLID 6 installation and imported into another. This file contains information concerning all (inter)related IUCLID 6 entities (documents and attachments), in a well-defined and structured format. This guide explains the structure of the IUCLID file in order for developers to build other systems than IUCLID 6 which can generate this format.
Download Part B – Developers' guide to the IUCLID format (.pdf)

Examples of PCN files are also provided both for single and group notifications.
Download a single notification example (197 KB | .i6z) and the corresponding IUCLID 6-generated report (132 KB|.pdf)
Download a group notifications example (188 KB | .i6z) and the corresponding IUCLID 6-generated report (156 KB|.pdf)

Latest events

Considerations for Deriving Health-Based Exposure Limits for Active Pharmaceutical Ingredients
19-21 June 2018, Intertek, Online Webinar

TSCA at 2: An Update on Implementation and Hot Topics
25 June 2018, Bergeson & Campbell, P.C., Webinar

Practical Risk Assessment Training
26-27 June 2018, Chemical Watch, Park Royal on Pickering

Risk Assessment for Biocides
4-5 September 2018, Chemical Watch, Le Chatelain, Bruxelles

Safer Chemicals in Products 2018
17-18 September 2018, Chemical Watch, Hyatt Regency Boston Harbor

CHCS Training "EU CLP (GHS) Classification for Supply - Mixtures" (Module 18)
31 October 2018, Chemical Hazards Communication Society (CHCS), London, United Kingdom

CHCS Training "EU CLP (GHS) Labelling for Supply" (Module 19)
1 November 2018, Chemical Hazards Communication Society (CHCS), London, United Kingdom

CHCS Training "Advanced Preparation of Safety Data Sheets" (Module 15)
6 November 2018, Chemical Hazards Communication Society (CHCS), London, United Kingdom

CHCS Training "Risk Characterisation and the Chemical Safety Report" (Module 53)
12 December 2018, Chemical Hazards Communication Society (CHCS), Manchester, United Kingdom

CHCS Training "The Extended SDS - Understanding Exposure Scenarios" (Module 20)
13 December 2018, Chemical Hazards Communication Society (CHCS), Manchester, United Kingdom

Chemsafe's staff wishes you a good and relaxed vacation

End of the Newsletter