29 NOVEMBER 2012

Responses to Comments Document (RCOM) on ECHA's Draft 4th Recommendation for 1,2-Dichloroethane (EC number: 203-458-1)

This document provides ECHA's responses to the comments received during the public consultation on the draft 4th recommendation for inclusion of substances in Annex XIV of REACH. In addition to this Response to Comments table, on ECHA's website there is available a zip-file including all attachments to the individual comments (as far as not confidential): http://echa.europa.eu/documents/10162/13640/axiv_rcom_edc_substances_attachments_en.7z

PUBLIC VERSION

CONTENT

I - General comments on the recommendation to include the substance in Annex XIV, including the prioritisation of the substance:

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
18	2012/09/20 00:58 See attachment *18_EDC comments BASF SE.doc*	BASF SE Company Germany	BASF SE Comments on the Prioritisation of 1,2-dichloroethane (EDC) The main use of EDC (around 8 million t/a) is as intermediate in the manufacture of VCM. The use as intermediate is not within the scope of authorisation. The main uses within the scope of authorisation are as a solvent, processing aid or extraction agent in the synthesis of agrochemicals, pharmaceuticals, plastics and other fine chemicals under strictly controlled conditions (SCC), as the diluted intermediates have to be handled under this way. Chemistry For a limited series of industrial syntheses in the sector of speciality chemicals 1,2-dichloroethane ("EDC") has been selected as solvent due to its stability against electrophilic attack, e.g. by agents like AlCl3, SO3, HSO3Cl and halogens. The use as solvent for such chemical reactions is often addressed in the patent literature, and in textbooks on preparative organic chemistry. EDC is also used in liquid-liquid extractions of synthetic and naturally occurring substances from aqueous media. Alternatives Often no better alternatives to EDC were found when these processes were optimized for production on a large scale, maintaining a high yield, purity and resource efficiency. A lot of work has been done to substitute EDC used as industrial solvent / extraction agent according to the carcinogens directive, which requires looking for replacement of carcinogenic agents classified as 1A or 1B. Substitution was successful for a very limited number of processes as EDC is a very efficient solvent, especially for extraction purposes. Also alternatives were involved which meanwhile are under scrutiny (see below). Technical process	Thank you for your comment and the additional information provided. This will be taken into account, where relevant, for finalisation of ECHA's recommendation of substances to be included in Annex XIV and the corresponding background documentation. **Regarding prioritisation of ECD or exemption for specific uses:** Topics such as the availability and suitability of alternatives, socio-economic considerations regarding the benefits of a use or the (adverse) impacts of ceasing a use as well as information on the low level of risk associated to a use are important. Information regarding these topics should be provided as part of the application for authorisation (e.g. in the analysis of alternatives, the chemical safety report or the socio-economic analysis). This information will be taken into account by the Risk Assessment and Socio-Economic Analysis Committees when forming their opinions and by the Commission when taking the final decision. It may impact the decision on granting the applied for authorisation and the conditions applicable to the authorisation, such as e.g. the length of the time limited review period of the authorisation. However, it is to be stressed that the prioritisation for the inclusion in Annex XIV is

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			EDC can be easily recycled and reused in the same facility or refined outside the facility for further use. Typically, the use of a certain tonnage of EDC leads to the production of a tonnage of product 300 times greater. In practical terms, this means that with 100 tonnes of EDC, 30,000 tonnes of product are produced under the usual controlled conditions for chemical processes. This factor arises from the efficiency provided by solvent recycling. The only demand is due to losses by discharging of the recycling waste. The waste is incinerated according to the waste legislation. Regulations and competitiveness EDC is listed in the European Pharmacopeia as a process solvent. It generally takes years to get the approval for a new solvent / a new process when the end product is an active substance either for pharmaceutical or for agrochemical applications as the registration legislation requests the registration of the entire production process. Registration means also new toxicological studies including mammals on a global scale as every country where the product is placed in the world requests an own registration. Though the result will be the same as for the studies before as only the processing solvent was changed without any effect in composition and subsequently toxicology of the purified end product. A major concern for European producers and users is competitiveness of the industry. As pharmaceutical and agrochemical production chains are registered from start to finish, in these cases authorization places costs on European producers and users that does not exist for non-EU producers. In addition as the outcome of an authorization is not clear it creates a high degree of uncertainty with regard to future investments. Another aspect is that the he EU-based industry will seek alternatives and try to register a new synthetic pathway, while non-EU firms can import the final product without extra costs, as the importation of finished products depends only on the final composition. This provides an incentive for manufacturers to seek non-EU solutions, to the detriment of EU industry. This problem is not limited to EDC, but includes other non-protic solvents such as NMP, DMAC and DMF, limiting the ability of EU industry to innovate. As the risk of only around 3,347 t/a in the described uses within the scope of authorisation are much smaller than the main volume outside the scope of authorisation and the number of sites (18) is by far lower and we have strictly controlled conditions (PROCS are not sufficient conclusive to deduct SCC), we propose alternative risk management options:	based on the criteria set out in Art 58(3) and follows the agreed approach described in the general approach document (http://echa.europa.eu/documents/10162/17232/axiv_priority_setting_gen_approach_20100701_en.pdf). Consequently information on topics such as the availability and suitability of alternatives, socio-economic considerations regarding the benefits of a use or the (adverse) impacts of ceasing a use as well as information on the low level of risk associated to a particular use are not considered in the prioritisation for recommending substances for inclusion Annex XIV. **Regarding authorisation with exemption:** See response to Comment 1 below. In addition, according to Art. 56(4) REACH, substances used in plant protection products within the scope of the relevant EU legislations are exempted from authorisation. Regulation 1107/2009 concerning the placing of plant protection products on the market includes a risk assessment and authorisation procedure for active substances and products containing these substances, including the relevant transitional measures applicable to certain provisions of Directive 91/414/EC. Under this Regulation, 1,2-dichloroethane is not an approved substance. Therefore, the exemption in Article 56(4)(a) REACH cannot apply. It needs to be examined whether an exemption can be granted under Article 58(2) REACH. Regulation 396/2005 sets maximum residue

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			Authorisation with exemption: Under authorisation non-intermediate industry uses of EDC under strictly controlled conditions should be exempted. This is analogous to the production of EDC and use of EDC as an intermediate in downstream plants . EDC is already not approved EU wide as active substance, safener, synergist, adjuvant or co-formulant under the plant protection regulation 1107/2009 and residual levels are defined under regulation 396/2005 for EDC EU-wide. BASF also does not use EDC in non-EU plant protection products. Agroproducts synthesised with EDC as solvent and approved according regulation 1107/2009 have, if defined by the approving authorities, maximum values for EDC as impurity. This is supported by the fact that EDC in the synthesis of agrochemicals, pharmaceuticals and plastics for food contact and medical devices is part of the specific European and global regulations. These highly regulated fields prohibit a switch away from EDC and establishs an interlinkage between international legislative requirements. Restriction EDC is already restricted by annex XVII REACH for consumer applications. The dossier describes the risk is 400 times higher than the value of 1 x 10-5, which is considered as acceptable lifetime cancer risk level for workers in the Guidance on Information Requirements and Chemical Safety Assessment (ECHA, 2008). In this case, a real risk for this non-threshold substance (up to now) exists, which then requires a restriction rather than an authorisation. This could be an extension of the existing annex XVII restriction similar to the dossier of the Netherlands for NMP defining EU wide harmonised occupational levels taking the 10-5 cancer risk level in consideration. Another alternative is a restriction allowing only industrial use under strictly controlled conditions (SCC). In any case industry is willing to support those alternative risk management options ensuring competitiveness and avoiding uncertainties for investments (also in even higher safety measures).	levels (MRLs) of pesticides in or on food and feed of plant and animal origin, to avoid that such residues present unacceptable risks to humans. MRLs have been set for 1,2-dichloroethane. While agroproducts synthesised with 1,2-dichloroethane as a solvent may have maximum levels set for 1,2-dichloroethane as an impurity, the plant protection product legislation does not appear to control risks to human health or the environment arising from the manufacturing stage of these products or, in particular, from the solvent use and disposal of 1,2-dichloroethane. Therefore, this legislation may not be regarded as a sufficient basis for exempting this use of 1,2-dichloroethane from authorisation in accordance with Article 58(2) of the REACH Regulation. **Regarding comment on restriction would be better option:** Please note that in the process of assessing whether a substance on the Candidate List has priority for inclusion in Annex XIV and therefore should be recommended for inclusion in this annex we are not in the position to assess alternative regulatory risk management options for the substance or its particular uses. **Regarding wrong score:** See response to Comment 11 below.

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17	2012/09/19 21:53	European Environmental Bureau (EEB) International NGO Belgium	The EEB supports the inclusion of this substance in Annex XIV due to its hazardous properties, high production volumes and wide spread uses. It is also a substance that is included in both the SIN List (http://www.sinlist.org/) and the Trade Union Priority List (http://www.etuc.org/a/6023) and cause occupational diseases. The use of this substance in the market is having adverse consequences for public health and environment and should be banned or severely restricted at European level.	Thank you for providing your opinion.
16	2012/09/19 21:29	ChemSec International NGO Sweden	We support the recommendation to include this substance in Annex XIV.	Thank you for providing your opinion.
15	2012/09/19 18:34	European Trade Union Confederation Trade union Belgium	ETUC supports the recommendation to include the substance in the authorisation list. This substancehttp://www.etuc.org/a/6023 is also included in the Trade Union Priority List for REACH authorisation. See	Thank you for providing your opinion.
14	2012/09/19 18:33	Company Germany	SR&D and precursor uses like filling and packaging of R&D chemicals are threatened by authorization. We would recommend an inclusion into annex XVII with restriction of the uses that have an impact on health and environment. We do not recommend including this substance in Annex XIV. We have further strong doubts on the number of sites that are using this substance. Before using this as an argument for wide dispersive use the number of sites using this substance should be properly evaluated	Thank you for your comment **Regarding SRD and precursor uses:** Please note that although uses for scientific research and development of a substance are exempted from the authorisation requirement in accordance with Article 56(3) this appears to only apply to its final use for SRD purposes under the conditions defined in Article 3(23). However, use of a CMR substance included in Annex XIV, on its own or in a mixture (above the lowest of the concentration limits specified in Directive 1999/45/EC or in Part 3 of Annex VI to Regulation (EC) No1272/2008), for e.g. refilling or packaging with the intention to supply them for SRD

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				purposes, would probably require authorisation. As 1,2-dichloroethane is a carcinogen, there is a strong societal interest to protect humans, in particular workers handling the substance, from risks potentially arising from its uses. An authorisation requirement for 1,2-dichloroethane will accordingly ensure that the health of workers in the EU involved in the uses of this substance is protected. **Regarding comment on restriction would be better option:** See response to comment 18 above **Regarding doubts on number of use sites:** See response to comment 11 below
13	2012/09/19 10:47	MSCA Sweden	We support the prioritisation of 1,2-dichloroethane for inclusion in Annex XIV. The substance has high priority due to high to very high volume and wide dispersive use.	Thank you for providing your opinion.
12	2012/09/18 21:48	Euroepan Federation of Pharmaceutical industries & Associations International organisation Switzerland	With ECHA's 4th recommendation published on 20th June 2012, the substance 1,2 –dichloroethane (EDC) was recommended for "prioritization for authorisation". This solvent has an important role for the production of and as an analytical standard for medicinal products. General comments on the recommendation to include 1,2 –dichloroethane (EDC) in Annex XIV, including the prioritisation of the substance 1,2-dichloroethane is mainly used as an intermediate in industrial manufacturing and production processes. Less than 1% of the total volume of 1,2-dichloroethane manufactured in the EU is for non-intermediate applications e.g. pharmaceutical or agrochemical production, where 1,2-dichloroethane is used as an industrial solvent,	Thank you for your comment and the additional information provided. This will be taken into account, where relevant, for finalisation of ECHA's recommendation of substances to be included in Annex XIV and the corresponding background documentation. **Regarding Art 58(2) exemption:** See response to comment 1 below

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			processing aid or extracting agent. The use of 1,2-dichloroethane as a solvent in scientific R&D processes (low amounts used only in professional laboratories for analytical quality control under laboratory conditions) are exempted from authorisation and will not be further discussed in the present annotation. Additionally the application of existing EU regulations to the use of 1,2-dichloroethane as a solvent under strictly controlled conditions in pharmaceutical production guarantees a high level of protection of human health and environment. Therefore, the use of 1,2-dichloroethane as solvent in pharmaceutical production under strictly controlled conditions should be exempted from authorisation. 1,2-dichloroethane is used as a solvent in a closed batch process, during the syntheses of active pharmaceutical ingredients. The life cycle of the substance at the downstream use facility normally involves the following distinctive steps: • Transfer of substance from road tanker to dedicated storage tank via contained piping, • Material transfer from bulk storage tank to reaction vessel, via contained piping, • Periodic cleaning and maintenance works under SCC, • Routine sampling via closed loop system, • Transfer of liquid waste stream from reaction vessels via contained piping to dedicated storage tanks, • Destruction of liquid waste stream by incineration as per an IPPC licence. Examples of other risk management measures communicated in the extended safety data sheet, which have been in place prior to registration of this substance: • Substance is handled only by trained personnel • In the case of cleaning and maintenance works, special procedures such as purging and flushing with a less hazardous solvent are applied before the system is opened and entered. Subsequent entry into the system requires a 'confined space permit', outlining specific safe conditions including acceptable atmospheric monitoring levels, which must be in place prior to entry. • Substance handling procedures are well documented and strictly supervised by the site operator. Additionally the manufacture of active pharmaceutical ingredients is performed within enclosed equipment in accordance with Good Manufacturing Practices (GMP). 1,2-dichloroethane (and other solvents) are introduced into the reactors via transfer systems designed to minimise environmental release, by trained personnel using appropriate protective equipment, and are thus contained within the process stream.	**Regarding Art 2(5) exemption:** According to Art. 2(5) REACH, substances used in medicinal products for human and veterinary use within the scope of the relevant EU legislation are exempted from the authorisation process. Please note that individual companies may benefit from the exemptions foreseen in Art. 2(5)(a) REACH if the conditions are met.

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			Since the residual amount of 1,2-dichloroethane in the eventual product (drug substance) is safety-limited by EMA (European Medicines Agency) guidance, in practice virtually all the 1,2-dichloroethane used during manufacture will be recycled and incinerated under strictly controlled conditions. Thus, the risks of environmental exposure of 1,2-dichloroethane in the pharmaceutical manufacturing environment are minimized by the equipment design and operational controls; disposal and record-keeping procedures exist within the oversight of the quality system. In Summary: It is not the intention of REACH to impact market availability of health care products that are adequately regulated through other European directives and regulations. This is underlined by, not only by Articles 2(5a) and 58(2) but also in Recital 111 stating: It is important to avoid confusion between the mission of the Agency and the respective missions of the European Medicines Agency (EMEA) established by Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency… As the use of solvents is covered specifically under the medical products legislation with specific limits for specific substances referring to that guideline, we claim that 1,2-dichloroethane, (CAS 107-06-2) to be exempted from Authorisation) in the production and analytics of medicinal products (including the production of intermediates to manufacture medicinal products). In addition we request an exemption for associated PPORD activities for up to 10 tonnes/pa	
11	2012/09/18 18:06 See attachment *11_Public comments 20120918 final.doc*	Industry or trade association Belgium	We have performed a survey of the registrants, and have refined the prioritisation calculation. The results of this is a lower prioritisation of 10, the details of which can be seen in the attached comments.	**Priority of ECD:** When applying the prioritisation approach for the 4th recommendation, ECHA took into account the information available from the registrations, Annex XV report and public commenting during SVHC identification. During the commenting period on the 4th

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				recommendation for inclusion in Annex XIV of 1,2-dichloroethane, the EDC REACH consortium provided the attached comments, inter alia on prioritisation, and the registrations were updated as well. In the attached comments it is stated that EDC might be given too high priority for inclusion in Annex XIV because of overestimation of the volume of the substance assigned to uses in the scope of authorisation and the wide-dispersiveness of the uses. Taking account of the comments, the priority of the substance has been re-assessed with the following results: Regarding the volume within the scope of authorisation, there was some uncertainty during prioritisation of 1,2-dichloroethane. From the registrations evidence was available that the volume was above 1000 t/y, however, the upper limit could not clearly be defined as in several registration dossiers no use specific volumes were given. Information provided by the EDC consortium and others during public consultation now indicates that the volume in the scope of authorisation is likely to be below 10,000 t/y. This means a volume score of 7 instead of the originally estimated range of 7-9. In the course of updating the registrations the following uses have been removed from the identified uses and included in the section of uses advised against: - Production of rubber - Formulation of degreasing solvents - Formulation of adhesives Remaining in the scope of authorisation are uses of EDC as a solvent, processing aid or

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				extraction agent, which according to information provided by the EDC REACH Consortium take place at 18 sites. Although this figure may not reflect the complete picture, the information provided indicates that the number is likely to be in the 10s rather than 100s (resulting in a score for the number of sites of 2 instead of previously 3). The EDC REACH Consortium concludes in its comments that the uses of 1,2-dichloroethane take place under strictly controlled conditions. However, even though some of the registrations include only processes indicating such strictly controlled conditions, other registrations and downstream user reports include processes indicating the likelihood of exposure. Due to the apparently very low DMEL of the substance, if calculated in line with the respective provisions of the guidance on information requirements[1], already relatively low releases are likely to be significant. Furthermore, the substance is highly volatile. In essence, there is indication of potential for significant exposure of workers and therefore the originally assigned release score of 3 is maintained. Taken together, the revised priority score of the substance is 14 instead of originally 17-

[1] The DMEL used in the registrations is based on a tolerable risk of 4 x 10^{-3}, whereas in accordance with the guidance on information requirements and chemical safety assessment (chapter R.8 (characterisation of dose [concentration]-response for human health) cancer risk levels of 1 x 10^{-5} and 1 x 10^{-6} could be seen as indicative tolerable risk levels when setting DMELs for workers and the general population, respectively. In the present case where the general population is not affected, the level of 10^{-5} should have been used. As indicated in the comments by the EDC REACH consortium, the risks described in the registration dossiers are 400 times higher than the value of 1 x 10^{-5}.

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				19. Suggestion to consider restriction: As regards the suggestion to consider restriction for the substance, please note that in the process of assessing whether a substance on the Candidate List has priority for inclusion in Annex XIV and therefore should be recommended for inclusion in this annex we are not in the position to assess the pertinence of alternative regulatory risk management options for the substance.
10	2012/09/18 17:59	INEOS Chlorvinyls Limited Company United Kingdom	We do not agree with the high prioritisation score since the number of sites invovled in using the substance in applications covered by authorisation is far lower than stated in the consultation document. New informaiton is available from registrants and this should be taken intoa ccount.	**Regarding prioritisation score of ECD:** See response to comment 11
9	2012/09/18 16:41	Association of the British Pharmaceutical Industry Industry or trade association United Kingdom	Background With ECHA's 4th recommendation published on 20th June 2012, the substance 1,2 –dichloroethane (EDC) was recommended for "prioritization for authorisation". This solvent has an important role for the production of and as an analytical standard for medicinal products. General comments on the recommendation to include 1,2 –dichloroethane (EDC) in Annex XIV, including the prioritisation of the substance 1,2-dichloroethane is mainly used as an intermediate in industrial manufacturing and production processes. Less than 1% of the total volume of 1,2-dichloroethane manufactured in the EU is for non-intermediate applications e.g. pharmaceutical or agrochemical production, where 1,2-dichloroethane is used as an industrial solvent, processing aid or extracting agent. The use of 1,2-dichloroethane as a solvent in scientific R&D processes (low amounts used only in professional laboratories for analytical quality control under laboratory conditions) are exempted from authorisation and will not be further discussed in the present annotation.	**See response to comment 12**

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			Additionally the application of existing EU regulations to the use of 1,2-dichloroethane as a solvent under strictly controlled conditions in pharmaceutical production guarantees a high level of protection of human health and environment. Therefore, the use of 1,2-dichloroethane as solvent in pharmaceutical production under strictly controlled conditions should be exempted from authorisation. 1,2-dichloroethane is used as a solvent in a closed batch process, during the syntheses of active pharmaceutical ingredients. The life cycle of the substance at the downstream use facility normally involves the following distinctive steps: • Transfer of substance from road tanker to dedicated storage tank via contained piping, • Material transfer from bulk storage tank to reaction vessel, via contained piping, • Periodic cleaning and maintenance works under SCC, • Routine sampling via closed loop system, • Transfer of liquid waste stream from reaction vessels via contained piping to dedicated storage tanks, • Destruction of liquid waste stream by incineration as per an IPPC licence. Examples of other risk management measures communicated in the extended safety data sheet, which have been in place prior to registration of this substance: • Substance is handled only by trained personnel • In the case of cleaning and maintenance works, special procedures such as purging and flushing with a less hazardous solvent are applied before the system is opened and entered. Subsequent entry into the system requires a 'confined space permit', outlining specific safe conditions including acceptable atmospheric monitoring levels, which must be in place prior to entry. • Substance handling procedures are well documented and strictly supervised by the site operator. Additionally the manufacture of active pharmaceutical ingredients is performed within enclosed equipment in accordance with Good Manufacturing Practices (GMP). 1,2-dichloroethane (and other solvents) are introduced into the reactors via transfer systems designed to minimise environmental release, by trained personnel using appropriate protective equipment, and are thus contained within the process stream. Since the residual amount of 1,2-dichloroethane in the eventual product (drug substance) is safety-limited by EMA (European Medicines Agency) guidance, in practice virtually all the 1,2-dichloroethane used during manufacture will be recycled and incinerated under strictly controlled conditions. Thus, the risks of environmental	

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			exposure of 1,2-dichloroethane in the pharmaceutical manufacturing environment are minimized by the equipment design and operational controls; disposal and record-keeping procedures exist within the oversight of the quality system.	
7	2012/09/18 14:45 See attachment *7_EDC DU WG comments 19-09-2012.doc*	EDC Downstream User Working Group Other contributor France	Please check the enclosed file	Thank you for your comment and the additional information provided. This will be taken into account, where relevant, for finalisation of ECHA's recommendation of substances to be included in Annex XIV and the corresponding background documentation. **Regarding prioritisation of 1,2-dichloroethane:** See response to comment 18 above **Regarding prioritisation score of ECD:** See response to comment 11 above **Regarding DMEL derivation and mechanism of action for carcinogenicity:** See response to comment 11 above **<u>Regarding Art 58(2) exemption:</u>** See response to comment 1 below
6	2012/09/17 22:18 See attachment *6_Section IV*	Company Ireland	The potential inclusion of 1,2-dichloroethane in Annex XIV is a significant concern for our company, a leading innovation driven provider of medicines that improve people's quality of life. Comments presented here should be considered in connection with the input provided by the European Federation of the Pharmaceutical industry (EFPIA). 1,2-dichloroethane is used at a pharmaceutical manufacturing facility under the	**<u>Regarding Art 58(2) exemption:</u>** See response to comment 1 below

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	Attachment_Comment.doc		strictly controlled conditions as prescribed by the chemical safety report. Identification of a suitable less hazardous alternative to 1,2-dichloroethane would require extensive redevelopment of the existing chemical process and require regulatory approval from health authorities globally in order to ensure product quality, efficacy and patient safety is not compromised. Scientific studies have shown that the 1,2-dichloroethane cannot be substituted with a less hazardous alternative. The use of 1,2-dichloroethane is critical to the formation of the desired crystal form of the active pharmaceutical ingredient. If an authorisation application was unsuccessful, in order to maintain an approved supply of medicine to patients the company will be forced to move the manufacturing process involving the use of 1,2-dichloroethane outside the EU. It is our opinion, that the use of 1,2-dichloroethane as a solvent in the production of medicinal products under strictly controlled conditions, should be exempt from authorisation as there is sufficient community legislation in place imposing minimum requirements relating to the protection of patients, workers and the environment.	**See also response to comment 12 above**
5	2012/09/17 20:07	Company Sweden	As a consequence of the inclusion of 1,2-Dichloroethane on the 4th draft recommendation of priority substances to be included in Annex XIV of the REACH Regulation that was published on June, 20th 2012, we would like to ensure that ECHA is familiar with certain critical uses of 1,2-Dichloroethane. We encourage ECHA to exempt from the authorization requirement the vital use of 1,2-Dichloroethane as a solvent during manufacture of fine chemicals used in the manufacture and purification of Active Pharmaceutical Ingredients. Information on our use: 1,2-Dichloroethane is used under strictly controlled conditions in closed systems as process chemical (solvent) during the manufacture of fine chemicals used in the Pharmaceutical and Biopharmaceutical industries. 1,2-Dichloroethane is used as a process chemical and thus is not part of the final fine chemical. There are currently no known technically equivalent substitutes for this use. The majority of the used substance is recycled in closed systems after being purged and recaptured in the production steps following its use. The rest of the substance is sent for incineration to a certified waste vendor. Use descriptors for our use of 1,2-Dichloroethane: • SU3 Industrial uses: Uses of substances as such or in preparations at industrial sites • SU9 Manufacture of fine chemicals – C20.5.9 Manufacture of other chemical	Thank you for your comment and the additional information provided. This will be taken into account, where relevant, for finalisation of ECHA's recommendation of substances to be included in Annex XIV and the corresponding background documentation. Information provided during the earlier consultation period has already been taken into account during priority setting and when preparing the draft recommendation. **Regarding prioritisation of ECD or exemption for specific uses:** See response to comment 18 above

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			products n.e.c • SU24 Scientific research and development. • PC0 Other – UCN code O15000 Solvents • PROC3 Use in closed batch process (synthesis or formulation) • PROC 8b Transfer of substance or preparation (charging/discharging) from/to vessel/large containers at dedicated facilities • ERC4 Industrial use of processing aids in processes and products, not becoming part of articles. No release of the substance to water, air or soil. 90% of the substance is recovered in solvent recovery plant. 10% becomes hazardous waste and is handled by authorized waste vendor. Occupational exposure is analyzed by taking samples and exposures are controlled by performing safety risk assessments and implementing mitigation measures. There are occupational exposure limit values for 1,2-Dichloroethane applicable to Sweden (level limit value 4 mg/m3) and our operations are routinely well below these values. Occupational exposure limit values for 1,2-Dichloroethane applicable in other member states are similar or higher than those applicable in Sweden. Therefore our operations are routinely well below the applicable occupational exposure limit values throughout the European Community. According to Regulation (EC) No 1272/20081,2-Dichloroethane is classified as a carcinogen category 1B, H350. In the confidential comments submitted we describe our uses in more details together with the controls used to protect the health and safety of employees in accordance with EU directives. Refer also to our previous comment during the consultation period before the inclusion of 1,2-Dichloroethane on the Candidate list, reference number dca6c034-77ed-45e8-a0dc-55ed4f034fe2.	
4	2012/09/17 19:41	European Council of Vinyl Manufacturers Industry or trade association Belgium	ECVM would like express surprise at the high priority given to EDC for addition to Annex XIV. In our view, this priority is not justified, for the following reasons: 1. More than 99 % of EDC is used to manufacture vinyl chloride monomer (VCM) and other chemical substances under "strictly controlled conditions", and hence qualifies as intermediate according to REACH. The amounts sold to industrial users for non-intermediate uses, the only ones relevant for Annex XIV, are only in the order of a few thousand tons per year. 2. As concluded by the Institute of Occupational Medicine in May 2011 less than 3,000 people are potentially exposed in Europe, most in the manufacture of VCM with about 500 exposed when 1,2-dichloroethane is used for other industrial uses. See	**Regarding prioritisation score of ECD:** See response to comment 11 above **Regarding questioning of classification:** 1,2-Dichloroethane (EC number: 203-458-1) has been identified as Substance of Very High Concern and included in the Candidate List of

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			memorandum " Health, socio-economic and environmental aspects of possible amendments to the EU Directive on the protection of workers from the risks related to exposure to carcinogens and mutagens at work, 1,2-Dichloroethane)" 3. The classification of EDC as carcinogen category 1B relies on one single study on rodents. The lack of epidemiological evidence for human carcinogenicity indicates a possible hormonal mechanism not relevant to humans. Further studies in preparation may well challenge the current classification.	substances for eventual inclusion in Annex XIV on 19/12/2011. The identification of the substance is based on its harmonised classification as a carcinogen, Carc. 1B, according to Annex VI, part 3, Table 3.1 of Regulation (EC) No 1272/2008. As the cited harmonised classification is applicable law at present, it will not be questioned or discussed in the context of this recommendation. Manufacturers, importers and downstream users who have new information which may lead to a change of the harmonised classification of a substance in Annex VI of Regulation (EC) No 1272/2008 may submit a revision proposal in accordance with the second subparagraph of Article 37(2) of Regulation 1272/2008 to the competent authority in one of the Member States in which the substance is placed on the market.
3	2012/09/17 18:32	Pharmachemical Ireland Industry or trade association Ireland	The majority of 1,2-dichloroethane (estimated at in excess of 99%) is used in Europe as an intermediate in industrial manufacturing and production processes. Given such usage and classification it is exempt under current legislation from the authorization process. Less than 1% of the total volume of 1,2-dichloroethane manufactured in the EU is for non-intermediate applications e.g. pharmaceutical or agrochemical production, where 1,2-dichloroethane is used as an industrial solvent, processing aid or extracting agent. The application of existing EU regulations to the use of 1,2-dichloroethane as a solvent under strictly controlled conditions in pharmaceutical production assures a high level of protection of human health and the environment. Therefore, the use of 1,2-dichloroethane as solvent in pharmaceutical production under strictly controlled conditions should be exempt from authorisation.	**Regarding prioritisation of ECD or exemption for specific uses:** See response to comment 18 above
2	2012/09/12 15:16	MSCA Norway	The Norwegian CA supports the prioritization of Strontium chromate for inclusion in Annex XIV.	Thank you for providing your opinion.

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
1	2012/09/11 15:31	Bayer HealthCare Company Germany	Request for an exemption from Authorization for the use of 1,2-dichloroethane (EDC) CAS 107-06-2 as a solvent in the production of Medicinal Products under strictly controlled conditions Background With ECHA's 4th recommendation published on 20th June 2012, the substance 1,2 –dichloroethane (EDC) was recommended for "prioritization for authorisation". This solvent has an important role for the production of and as an analytical standard for, medicinal products. General comments on the recommendation to include 1,2 –dichloroethane (EDC) in Annex XIV, including the prioritisation of the substance 1,2-dichloroethane is mainly used as an intermediate in industrial manufacturing and production processes. Less than 1% of the total volume of 1,2-dichloroethane manufactured in the EU is for non-intermediate applications e.g. pharmaceutical or agrochemical production, where 1,2-dichloroethane is used as an industrial solvent, processing aid or extracting agent. The use of 1,2-dichloroethane as a solvent in scientific R&D processes (low amounts used only in professional laboratories for analytical quality control under laboratory conditions) are exempted from authorisation and will not be further discussed in the present annotation. Additionally the application of existing EU regulations to the use of 1,2-dichloroethane as a solvent under strictly controlled conditions in pharmaceutical production guarantees a high level of protection of human health and environment. Therefore, the use of 1,2-dichloroethane as solvent in pharmaceutical production under strictly controlled conditions should be exempted from authorisation. 1,2-dichloroethane is used as a solvent in a closed batch process, during the syntheses of active pharmaceutical ingredients. The life cycle of the substance at the downstream use facility normally involves the following distinctive steps: • Transfer of substance from road tanker to dedicated storage tank via contained piping, • Material transfer from bulk storage tank to reaction vessel, via contained piping, • Periodic cleaning and maintenance works under SCC, • Routine sampling via closed loop system, • Transfer of liquid waste stream from reaction vessels via contained piping to	Thank you for your comment. **<u>Regarding Art 2(5) exemption:</u>** See response to comment 12 above **<u>Regarding Art 58(2) exemption:</u>** According to Article 58(2) of REACH it is possible to exempt from the authorisation requirement uses or categories of uses 'provided that, on the basis of the existing specific Community legislation imposing minimum requirements relating to the protection of human health or the environment for the use of the substance, the risk is properly controlled'. ECHA considers the following elements when deciding whether to include an exemption of a use of a substance in its recommendation: - There is existing EU legislation addressing the use (or categories of use) that is proposed to be exempted. Special attention has to be paid to the definition of use in the legislation in question, compared to the REACH definitions in accordance with Art. 3(24). Furthermore, the reasons for and effect of any exemptions from the requirements set out in the legislation have to be assessed; - This EU legislation properly controls the risks to human health and/or the environment from the use of the substance arising from the intrinsic properties of the substance that are

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			dedicated storage tanks, • Destruction of liquid waste stream by incineration as per an IPPC licence. Examples of other risk management measures communicated in the extended safety data sheet, which have been in place prior to registration of this substance: • Substance is handled only by trained personnel • In the case of cleaning and maintenance works, special procedures such as purging and flushing with a less hazardous solvent are applied before the system is opened and entered. Subsequent entry into the system requires a 'confined space permit', outlining specific safe conditions including acceptable atmospheric monitoring levels, which must be in place prior to entry. • Substance handling procedures are well documented and strictly supervised by the site operator. Additionally the manufacture of active pharmaceutical ingredients is performed within enclosed equipment in accordance with Good Manufacturing Practices (GMP). 1,2-dichloroethane (and other solvents) are introduced into the reactors via transfer systems designed to minimise environmental release, by trained personnel using appropriate protective equipment, and are thus contained within the process stream. Since the residual amount of 1,2-dichloroethane in the eventual product (drug substance) is safety-limited by EMA (European Medicines Agency) guidance, in practice virtually all the 1,2-dichloroethane used during manufacture will be recycled and incinerated under strictly controlled conditions. Thus, the risks of environmental exposure of 1,2-dichloroethane in the pharmaceutical manufacturing environment are minimized by the equipment design and operational controls; disposal and record-keeping procedures exist within the oversight of the quality system. Uses (or categories of uses) to be exempted from the authorisation requirement Process categories applicable to the use(s) or categories of uses that are proposed to be exempted: PROC3 Use in closed batch process (synthesis or formulation)	specified in Annex XIV; generally, the legislation in question should specifically refer to the substance to be included in Annex XIV either by naming the substance or by referring to the group the substance belongs to, e.g. by referring to the classification criteria or the Annex XIII criteria; - This EU legislation imposes minimum requirements[2] for the control of risks of the use. Legislation setting only the aim of imposing measures or not clearly specifying the actual type and effectiveness of measures to be implemented is not regarded as sufficient to meet the requirements under Article 58(2). Furthermore, it can be implied from the REACH Regulation that attention should be paid as to whether and how the risks related to the life-cycle stages resulting from the uses in question (i.e. service-life of articles and waste stage(s) as relevant) are covered by the legislation. On the basis of the criteria above, we made the following observations on the argumentation brought forward by the commenting party: (i) Only existing EU legislation is relevant in the context to be assessed (no national

[2] Legislation imposing minimum requirements means that:
- The Member States may establish more stringent but not less stringent requirements when implementing the specific EU legislation in question.
- The piece of legislation has to define the measures to be implemented by the actors and to be enforced by authorities in a way that ensures the same minimum level of control of risks throughout the EU and that this level can be regarded as appropriate.

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			PROC8b Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities. PROC15: Use as a laboratory reagent Exemption from authorisation is requested for the use of 1,2-dichloroethane in the production of medicinal products as defined in Art. 1(2) of the Directive 2001/83/EC relating to medicinal products for human use and in the production of veterinary products as defined in Art. 1(2) Directive 2001/82/EC for medicinal products for animal use, as outlined in REACH Art. 58(1)e. Exemption from authorisation is also requested for the use of 1,2-dichloroethane up to 100 tonnes/pa regarding Process Orientated Research and Development (PPORD) covering PPORD relating to production of medicinal products for human and veterinary uses as outlined in REACH Art. 56(3) Rationale for the Request for an Exemption as per Article 58(2) REACh Art 58(2) confirms the following: Uses or categories of uses may be exempted from the authorisation requirement provided that, on the basis of the existing specific Community legislation imposing minimum requirements relating to the protection of human health or the environment for the use of the substance, the risk is properly controlled. In the establishment of such exemptions, account shall be taken, in particular, of the proportionality of risk to human health and the environment related to the nature of the substance, such as where the risk is modified by the physical form. The relevant existing EC regulations are: Directive 2001/83/EC & Regulation (EC) No 726/2004 The use of 1,2-dichloroethane in the manufacture of an active pharmaceutical ingredient(s) falls within the scope of Regulation (EC) No 726/2004 and Directive 2001/83/EC, relating to medicinal products for human use. The holder of a manufacturing authorisation of a medicinal product referred to in Article 40 of Directive 2001/83/EC is obliged "to comply with the principles and guidelines of GMP" as laid down by community law. Principles and guidelines of good manufacturing practice require impurity testing of pharmaceutical ingredients to ensure that specific threshold limits for residual solvents are met. EMA (European Medicines Agency) guidance on residual solvents (EMA/CHMP/ICH/82260/2006) contains a specific	legislation). (ii) Minimum requirements for controlling risks to human health or (and) the environment need to be imposed in a way that they cover the life cycle stages that are exerting the risks resulting from the uses in question. (iii) There need to be binding and enforceable minimum requirements in place for the substance(s) used. The relevant EU legislation referred to by the commenting party is assessed below. Regulation (EC) No 726/2004 establishes the operation of European authorisation procedures for the placing of medicinal products on the market in the European Union (EU). Each application for authorisation must be accompanied by the particulars and documents referred to in Directive 2001/83/EC on the Community code relating to medicinal products for human use or in Directive 2001/82/EC relating to the production, placing on the market, labelling, distribution and advertising of veterinary medicinal products. Whilst measures may be in place to control the residual amount of solvents in the final product, these pieces of legislation may not control risks to human health or the environment arising from the use of the substance at manufacturing stage of these products or, in particular, from the use and disposal of 1,2-dichloroethane. Therefore, they may be not regarded as a sufficient basis for exempting uses of 1,2-dichloroethane from authorisation in accordance with Article

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			concentration limit for 1,2-dichloroethane. Since the residual amount of 1,2-dichloroethane in the eventual product (drug substance) is safety-limited by the EMA (Guideline for Residual Solvents), in practice virtually all the 1,2-dichloroethane used during manufacture would be present in the waste streams that are then disposed in accordance with local environmental regulations. Thus, the risks of environmental exposure of 1,2-dichloroethane in the pharmaceutical manufacturing environment are minimized by the equipment design and operational controls; disposal and record-keeping procedures exist within the oversight of the quality system. As the use of solvents is covered specifically under the medical products legislation with specific limits for specific substances referring to that guideline, we claim the mentioned substance to be exempted from Authorisation in the production and analytics of medicinal products (including the production of intermediates to manufacture medicinal products). In addition we request an exemption for associated PPORD activities up to 100 tonnes/pa. 1999/13/EC Solvent Emissions Directive High Volume solvents (>50ts/yr) used in the Manufacture of Pharmaceutical Products are regulated under the Solvent Emissions Directive 1999/13/EC (as amended by 2004/42/EC) The purpose of the Solvent Emissions Directive is to prevent or reduce the direct and indirect effects of emissions of volatile organic compounds into the environment, mainly into air, and the potential risks to human health, by providing measures and procedures to be implemented for certain activities. Manufacture of Pharmaceutical Products is covered under Annex I (Scope) and the volumes under Annex IIA (thresholds and Emission Controls). 2004/37/EC Carcinogens and Mutagens Directive: The more stringent and/or specific provisions contained in the Carcinogens and Mutagens Directive (2004/37/EC) apply in addition to the requirements of the chemical agents directive 98/24/EC. Directive 2004/37/EC goes further, requiring an employer to use "existing appropriate procedures for the measurement of carcinogens", to assess the effectiveness of any preventative measures taken to protect the health and safety of workers. Downstream users are required by both community and national legislation not to exceed an exposure limit for a carcinogen. The Carcinogens and Mutagens Directive (2004/37/EC) requires that workplace exposures are avoided/minimised as far as technically possible. This legislation clearly specifies the actual type and effectiveness of measures to be implemented; of	58(2) of the REACH Regulation. The Carcinogens or Mutagens at Work Directive 2004/37/EC (CMD) introduces a framework of general principles to protect workers against risks to their health (which includes prevention of risk) from exposure. The overriding principle is that the employer shall reduce the use of a carcinogen or mutagen (CM) at the place of work, in particular by replacing it, in so far as is technically possible, by a substance, preparation or process which, under its condition of use, is not dangerous or is less dangerous to workers' health and safety. Where substitution is not possible, CMs should be used in closed systems, where technically possible. Furthermore, a hierarchy of measures shall be applied when a CM is used. The Directive outlines a hierarchy of control and risk reduction measures (with substitution at the top), however, it leaves the determination of the measures to be imposed to the employer and does not provide sufficient indicators to be used to assess whether a measure higher up in the hierarchy would have been technically possible. On this basis it is not considered that CMD would impose binding minimum requirements for controlling risks to human health. Therefore, this Directive may not be regarded as a sufficient basis for exempting uses of 1,2-dichloroethane from authorisation in accordance with Article 58(2) of the REACH Regulation. Directive 2010/75/EU on industrial emissions

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			particular note is Article 5(2): Where it is not technically possible to replace the carcinogen or mutagen by a substance, preparation or process which, under its conditions of use, is not dangerous or is less dangerous to health or safety, the employer shall ensure that the carcinogen or mutagen is, in so far as is technically possible, manufactured and used in a closed system. Therefore, the use of 1,2-dichloroethane as a solvent in pharmaceutical production under strictly controlled conditions meets the intent of Article 5(2) of Directive (2004/37/EC). As REACH does not overrule the Carcinogens and Mutagens Directive, this approach to controlling workplace exposure is regarded as the minimum requirement applied during the proposed use of 1,2-dichloroethane to be exempted. In addition, there is existing regulation concerning the incineration of waste: 2000/76/EC Waste Incineration Directive: Destruction of liquid waste solvents is by incineration, and is normally regulated by an IPPC licence. This requires the unit to be operated under the conditions of the Waste Incineration Directive (2000/76/EC) thus meeting all associated emission limit values to both air and water. In Summary: It is not the intention of REACH to impact market availability of health care products that are adequately regulated through other European directives and regulations. This is underlined by, not only by Articles 2(5a) and 58(2) but also in Recital 111 stating: It is important to avoid confusion between the mission of the Agency and the respective missions of the European Medicines Agency (EMEA) established by Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency… As the use of solvents is covered specifically under the medical products legislation with specific limits for specific substances referring to that guideline, we claim that 1,2-dichloroethane, (CAS 107-06-2) to be exempted from Authorisation) in the production and analytics of medicinal products (including the production of	(IED), (which will replace a number of existing Directives, including the IPPC Directive (2008/1/EC), the Solvents Emissions Directive (1999/13/EC) and the Waste Incineration Directive (2000/76/EC) from 7 January 2014), includes the provision that installations using organic solvents and undertaking activities listed in Annex VII, where applicable reaching specified consumption thresholds, should operate only if they hold a permit or are registered. More generally, IED Directive requirements apply to facilities engaged in production on an industrial scale of pharmaceutical products including intermediates. The Directive encourages substitution/reduction in usage of organic solvents and sets down emission limit values for particular activities (including manufacturing of pharmaceutical products) to protect human health and the environment. Under Article 58 IED Directive, volatile organic compounds (VOCs) such as 1,2-dichloroethane which are assigned or need to carry the hazard statement H350 (i.e. carcinogen 1B) '(…) shall be replaced, as far as possible by less harmful substances or mixtures within the shortest possible time'. Furthermore, according to Art 59(5) IED Directive, VOCs such as 1,2-dichloroethane which are assigned or need to carry the hazard statement H350, '(…) shall be controlled under contained conditions as far as technically and economically feasible to safeguard public health and the environment and shall not exceed the relevant emission limit values in Part 4 of Annex VII'.

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			intermediates to manufacture medicinal products). In addition we request an exemption for associated PPORD activities for up to 10 tonnes/pa	The emission limits stated in the IED Directive are by reference to activities using greater than certain tonnages/mass flow of solvent, while the authorisation requirement does not have a tonnage limit. In this respect, the provisions in this Directive may not cover all uses of this substance in pharmaceutical manufacturing subject to the authorisation requirement. The requirements relating to Waste Incineration under the IED Directive contribute to environmental protection at the waste life cycle stage. However, there does not appear to be sufficient protection of workers / man via the environment at other life cycle stages as outlined above. **Regarding PPORD exemption:** The authorisation title requests in Art. 55 the progressive replacement of SVHCs where this is technically and economically viable. Therefore, PPORD should in principle focus on alternative substances and technologies to replace the SVHC in question. However, we agree that in cases where no alternatives are available to replace the SVHC, PPORD with the aim to reduce the use of the substance or of its emissions could be justified. The pertinence of such a PPORD project with a substance identified as SVHC should however be justified in an authorisation application and be scrutinized and decided in the authorisation granting process in accordance with Article 60.

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response

II - Transitional arrangements. Comments on the proposed dates:

#	Date	Submitted by (name, Organisation/MSCA)	Comment	Response
17	2012/09/19 21:53	European Environmental Bureau (EEB) International NGO Belgium	As soon as possible	Thank you for your comment. ECHA made its proposals for the latest application dates on the basis of discussions by the stakeholder expert group that was following the development of the Guidance for including substances in Annex XIV. This expert group estimated that the time needed for preparation of an authorisation application of sufficient quality might in standard cases require 18 months (roughly 12 months worktime for drafting the application plus an additional buffer of 6 months for consulting required external expertise). As there is yet no reliable information available that would suggest shortening or prolonging this time interval, we consider that a period of 18 months should normally be given to allow for the preparation of a well documented application for authorisation. The anticipated workload of the Agency with regard to processing of authorisation applications was accounted for by grouping the proposed substances in 3 groups and spreading the application and sunset dates over a period of six months. Please note that the REACH Committee agreed in its meeting of 21/22 November 2012 that the latest application dates for the chromium(VI) substances included in the 3rd Recommendation should be set to 35 months after EiF of the inclusion of these substances into Annex XIV (anticipated to be in March 2013). In order to allow consistency amongst all chromium(VI) substances recommended for inclusion in the Authorisation List, the latest application dates for the chromium(VI) substances of the 4th Recommendation are therefore set to 24 months after EiF of their inclusion in Annex XIV (anticipated to be in February 2014). The latest application date for all chromium(VI) substances of the 3rd and 4th Recommendation will then consistently be February 2016.

				This adjustment of the LAD for the chromium(VI) substances requires a re-organisation of the LADs of the other substances of the 4th Recommendation in order to account for an appropriate distribution of the workload in the time provided for. Therefore, it is suggested to change the LADs for 1,2-dichloroethane to 21 months after EiF.
5	2012/09/17 20:07	Company Sweden	As stated in the Annex XV dossier by the Slovak Competent Authority (August 2011, part II, paragraph 2.2), "according to information from pharmaceutical industry using the substance as solvent/reagent in the manufacture of an Active Pharmaceutical ingredient, currently it is not feasible to substitute 1,2-DCE with a less hazardous alternative for both technical and economic reasons. Substitution of the substance with a less hazardous solvent/reagent would involve development of an alternative chemical synthetic route. Pharmaceutical industry is already subject to a very high degree of regulation, which provides a high level of protection for workers, the environment and patients". In addition, as acknowledged by ECHA in the draft background document for 1,2-dichloroethane (June 2012), "the Annex XV report (2011) does not provide detailed information on alternatives to EDC for its use as a solvent. It is stated that industry is making efforts to substitute EDC, where possible. However, it might be difficult to develop alternatives for some specific applications, particularly in the pharmaceutical industry". In addition, the use of 1,2-dichloroethane as an intermediate in fine chemical synthesis and as a solvent in chemical and pharmaceutical industries represents only around 0.2 % of the total used amounts. In the light of these comments and considering that our use of 1,2-dichloroethane is as process chemical (solvent) for the manufacture of fine chemicals used in the Pharmaceutical and Biopharmaceutical industries, we would like the period for application for authorization set to 60 months after date of inclusion in Annex XIV, instead of the proposed 24 months, in case our use of 1,2-Dichloroethane as process chemical for the manufacture of fine chemicals used in the Pharmaceutical and Biopharmaceutical industries would not be exempt from the authorization requirement. Difficulty to develop alternatives for this very specific application, is the reason why we would like a longer period for application for authorization to be able to explore less hazardous alternatives to 1,2-dichloroethane and validate them in our manufacturing processes.	Thank you for your comment. Please note that authorisation, *inter alia*, is a means to promote the development of alternatives. Article 55 explicitly stipulates that applicants for authorisation shall analyse the availability of alternatives and consider their risks, and the technical and economic feasibility of substitution (this has to be included in the analysis of alternatives to be submitted as part of the authorisation application in accordance with Art. 62 (4e)). Therefore, the present lack of alternatives to (some of) the uses of a substance and the need to complete R&D programmes to get qualified alternatives to it is no viable reason for adjourning the subjection of a substance or some of its uses to authorisation. Information regarding lack of alternatives is however important information for inclusion in an authorisation application. This information will be taken into account by the Risk Assessment and Socio-Economic Analysis Committees when forming their opinions and by the Commission when taking the final decision. It may impact the decision on granting the applied for authorisation and the conditions applicable to the authorisation, such as e.g. the length of the time limited review period of the authorisation.

III - Comments on uses that should be exempted from authorisation, including reasons for that:

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
18	2012/09/20 00:58	BASF SE Company Germany	Authorisation with exemption: Under authorisation non-intermediate industry uses of EDC under strictly controlled conditions should be exempted. This is analogous to the production of EDC and use of EDC as an intermediate in downstream plants . EDC is already not approved EU wide as active substance, safener, synergist, adjuvant or co-formulant under the plant protection regulation 1107/2009 and residual levels are defined under regulation 396/2005 for EDC EU-wide. BASF also does not use EDC in non-EU plant protection products. Agroproducts synthesised with EDC as solvent and approved according regulation 1107/2009 have, if defined by the approving authorities, maximum values for EDC as impurity. This is supported by the fact that EDC in the synthesis of agrochemicals, pharmaceuticals and plastics for food contact and medical devices is part of the specific European and global regulations. These highly regulated fields prohibit a switch away from EDC and establishs an interlinkage between international legislative requirements.	**See response to comment 18 in section I.**
16	2012/09/19 21:29	ChemSec International NGO Sweden	Being such a hazardous substance, no use should be granted a generic exemption from authorisation.	Thank you for your opinion.
12	2012/09/18 21:48	Euroepan Federation of Pharmaceutical industries & Associations International organisation Switzerland	Uses (or categories of uses) to be exempted from the authorisation requirement Process categories applicable to the use(s) or categories of uses that are proposed to be exempted: PROC3 Use in closed batch process (synthesis or formulation) PROC8b Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities. PROC15: Use as a laboratory reagent	**Regarding exemption for processes under strictly controlled conditions** See response to comment 18 in section I **Regarding exemption based on medicinal and veterinary regulations** See response to comment 1 in section I

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			Exemption from authorisation is requested for the use of 1,2-dichloroethane in the production of medicinal products as defined in Art. 1(2) of the Directive 2001/83/EC relating to medicinal products for human use and in the production of veterinary products as defined in Art. 1(2) Directive 2001/82/EC for medicinal products for animal use, as outlined in REACH Art. 58(1)e. Exemption from authorisation is also requested for the use of 1,2-dichloroethane up to 10 tonnes/pa regarding Process Orientated Research and Development (PPORD) covering PPORD relating to production of medicinal products for human and veterinary uses as outlined in REACH Art. 56(3) Rationale for the Request for an Exemption as per Article 58(2) REACh Art 58(2) confirms the following: Uses or categories of uses may be exempted from the authorisation requirement provided that, on the basis of the existing specific Community legislation imposing minimum requirements relating to the protection of human health or the environment for the use of the substance, the risk is properly controlled. In the establishment of such exemptions, account shall be taken, in particular, of the proportionality of risk to human health and the environment related to the nature of the substance, such as where the risk is modified by the physical form. The relevant existing EC regulations are: Directive 2001/83/EC & Regulation (EC) No 726/2004 The use of 1,2-dichloroethane in the manufacture of an active pharmaceutical ingredient(s) falls within the scope of Regulation (EC) No 726/2004 and Directive 2001/83/EC, relating to medicinal products for human use. The holder of a manufacturing authorisation of a medicinal product referred to in Article 40 of Directive 2001/83/EC is obliged "to comply with the principles and guidelines of GMP" as laid down by community law. Principles and guidelines of good manufacturing practice require impurity testing of pharmaceutical ingredients to ensure that specific threshold limits for residual solvents are met. EMA (European Medicines Agency) guidance on residual solvents	**Regarding PPORD exemption:** See response to comment 1 in section I

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			(EMA/CHMP/ICH/82260/2006) contains a specific concentration limit for 1,2-dichloroethane. Since the residual amount of 1,2-dichloroethane in the eventual product (drug substance) is safety-limited by the EMA (Guideline for Residual Solvents), in practice virtually all the 1,2-dichloroethane used during manufacture would be present in the waste streams that are then disposed in accordance with local environmental regulations. Thus, the risks of environmental exposure of 1,2-dichloroethane in the pharmaceutical manufacturing environment are minimized by the equipment design and operational controls; disposal and record-keeping procedures exist within the oversight of the quality system. As the use of solvents is covered specifically under the medical products legislation with specific limits for specific substances referring to that guideline, we claim the mentioned substance to be exempted from Authorisation in the production and analytics of medicinal products (including the production of intermediates to manufacture medicinal products). In addition we request an exemption for associated PPORD activities up to 10 tonnes/pa. 1999/13/EC Solvent Emissions Directive High Volume solvents (>50ts/yr) used in the Manufacture of Pharmaceutical Products are regulated under the Solvent Emissions Directive 1999/13/EC (as amended by 2004/42/EC) The purpose of the Solvent Emissions Directive is to prevent or reduce the direct and indirect effects of emissions of volatile organic compounds into the environment, mainly into air, and the potential risks to human health, by providing measures and procedures to be implemented for certain activities. Manufacture of Pharmaceutical Products is covered under Annex I (Scope) and the volumes under Annex IIA (thresholds and Emission Controls). 2004/37/EC Carcinogens and Mutagens Directive: The more stringent and/or specific provisions contained in the Carcinogens and Mutagens Directive (2004/37/EC) apply in addition to the requirements of the chemical agents directive 98/24/EC. Directive 2004/37/EC goes further, requiring an employer to use "existing appropriate procedures for the measurement of carcinogens", to assess the effectiveness of any preventative measures taken to protect the health and safety of workers. Downstream users are required by both community and national legislation not to exceed an exposure limit for a carcinogen. The Carcinogens and Mutagens Directive	

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			(2004/37/EC) requires that workplace exposures are avoided/minimised as far as technically possible. This legislation clearly specifies the actual type and effectiveness of measures to be implemented; of particular note is Article 5(2): Where it is not technically possible to replace the carcinogen or mutagen by a substance, preparation or process which, under its conditions of use, is not dangerous or is less dangerous to health or safety, the employer shall ensure that the carcinogen or mutagen is, in so far as is technically possible, manufactured and used in a closed system. Therefore, the use of 1,2-dichloroethane as a solvent in pharmaceutical production under strictly controlled conditions meets the intent of Article 5(2) of Directive (2004/37/EC). As REACH does not overrule the Carcinogens and Mutagens Directive, this approach to controlling workplace exposure is regarded as the minimum requirement applied during the proposed use of 1,2-dichloroethane to be exempted. In addition, there is existing regulation concerning the incineration of waste: 2000/76/EC Waste Incineration Directive: Destruction of liquid waste solvents is by incineration, and is normally regulated by an IPPC licence. This requires the unit to be operated under the conditions of the Waste Incineration Directive (2000/76/EC) thus meeting all associated emission limit values to both air and water.	
10	2012/09/18 17:59	INEOS Chlorvinyls Limited Company United Kingdom	It is known that this substance is used in pharmaceutical processes manufacturing key medications and inother chemical processes where the whole process is subject to regulation. Both of these could be considered under Article 58.2	**See response to comment 18 in section I**
9	2012/09/18 16:41	Association of the British Pharmaceutical Industry Industry or trade association United Kingdom	Uses (or categories of uses) to be exempted from the authorisation requirement Process categories applicable to the use(s) or categories of uses that are proposed to be exempted: PROC3 Use in closed batch process (synthesis or formulation) PROC8b Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities.	**Regarding exemption for processes under strictly controlled conditions** See response to comment 18 in section I **Regarding exemption based on medicinal and veterinary regulations**

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			PROC15: Use as a laboratory reagent Exemption from authorisation is requested for the use of 1,2-dichloroethane in the production of medicinal products as defined in Art. 1(2) of the Directive 2001/83/EC relating to medicinal products for human use and in the production of veterinary products as defined in Art. 1(2) Directive 2001/82/EC for medicinal products for animal use, as outlined in REACH Art. 58(1)e. Exemption from authorisation is also requested for the use of 1,2-dichloroethane up to 10 tonnes/pa regarding Process Orientated Research and Development (PPORD) covering PPORD relating to production of medicinal products for human and veterinary uses as outlined in REACH Art. 56(3) Rationale for the Request for an Exemption as per Article 58(2) REACh Art 58(2) confirms the following: Uses or categories of uses may be exempted from the authorisation requirement provided that, on the basis of the existing specific Community legislation imposing minimum requirements relating to the protection of human health or the environment for the use of the substance, the risk is properly controlled. In the establishment of such exemptions, account shall be taken, in particular, of the proportionality of risk to human health and the environment related to the nature of the substance, such as where the risk is modified by the physical form. The relevant existing EC regulations are: Directive 2001/83/EC & Regulation (EC) No 726/2004 The use of 1,2-dichloroethane in the manufacture of an active pharmaceutical ingredient(s) falls within the scope of Regulation (EC) No 726/2004 and Directive 2001/83/EC, relating to medicinal products for human use. The holder of a manufacturing authorisation of a medicinal product referred to in Article 40 of Directive 2001/83/EC is obliged "to comply with the principles and guidelines of GMP" as laid down by community law. Principles and guidelines of good manufacturing practice require impurity testing of pharmaceutical	See response to comment 1 in section I **Regarding PPORD exemption:** See response to comment 1 in section I

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			ingredients to ensure that specific threshold limits for residual solvents are met. EMA (European Medicines Agency) guidance on residual solvents (EMA/CHMP/ICH/82260/2006) contains a specific concentration limit for 1,2-dichloroethane. Since the residual amount of 1,2-dichloroethane in the eventual product (drug substance) is safety-limited by the EMA (Guideline for Residual Solvents), in practice virtually all the 1,2-dichloroethane used during manufacture would be present in the waste streams that are then disposed in accordance with local environmental regulations. Thus, the risks of environmental exposure of 1,2-dichloroethane in the pharmaceutical manufacturing environment are minimized by the equipment design and operational controls; disposal and record-keeping procedures exist within the oversight of the quality system. As the use of solvents is covered specifically under the medical products legislation with specific limits for specific substances referring to that guideline, we claim the mentioned substance to be exempted from Authorisation in the production and analytics of medicinal products (including the production of intermediates to manufacture medicinal products). In addition we request an exemption for associated PPORD activities up to 100 tonnes/pa. 1999/13/EC Solvent Emissions Directive High Volume solvents (>50ts/yr) used in the Manufacture of Pharmaceutical Products are regulated under the Solvent Emissions Directive 1999/13/EC (as amended by 2004/42/EC) The purpose of the Solvent Emissions Directive is to prevent or reduce the direct and indirect effects of emissions of volatile organic compounds into the environment, mainly into air, and the potential risks to human health, by providing measures and procedures to be implemented for certain activities. Manufacture of Pharmaceutical Products is covered under Annex I (Scope) and the volumes under Annex IIA (thresholds and Emission Controls). 2004/37/EC Carcinogens and Mutagens Directive: The more stringent and/or specific provisions contained in the Carcinogens and Mutagens Directive (2004/37/EC) apply in addition to the requirements of the chemical agents directive 98/24/EC. Directive 2004/37/EC goes further, requiring an employer to use "existing appropriate procedures for the measurement of carcinogens", to assess the effectiveness of any preventative measures taken to protect the health and safety of workers. Downstream	

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			users are required by both community and national legislation not to exceed an exposure limit for a carcinogen. The Carcinogens and Mutagens Directive (2004/37/EC) requires that workplace exposures are avoided/minimised as far as technically possible. This legislation clearly specifies the actual type and effectiveness of measures to be implemented; of particular note is Article 5(2): Where it is not technically possible to replace the carcinogen or mutagen by a substance, preparation or process which, under its conditions of use, is not dangerous or is less dangerous to health or safety, the employer shall ensure that the carcinogen or mutagen is, in so far as is technically possible, manufactured and used in a closed system. Therefore, the use of 1,2-dichloroethane as a solvent in pharmaceutical production under strictly controlled conditions meets the intent of Article 5(2) of Directive (2004/37/EC). As REACH does not overrule the Carcinogens and Mutagens Directive, this approach to controlling workplace exposure is regarded as the minimum requirement applied during the proposed use of 1,2-dichloroethane to be exempted. In addition, there is existing regulation concerning the incineration of waste: 2000/76/EC Waste Incineration Directive: Destruction of liquid waste solvents is by incineration, and is normally regulated by an IPPC licence. This requires the unit to be operated under the conditions of the Waste Incineration Directive (2000/76/EC) thus meeting all associated emission limit values to both air and water. In Summary: It is not the intention of REACH to impact market availability of health care products that are adequately regulated through other European directives and regulations. This is underlined by, not only by Articles 2(5a) and 58(2) but also in Recital 111 stating: It is important to avoid confusion between the mission of the Agency and the respective missions of the European Medicines Agency (EMEA) established by Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and	

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			establishing a European Medicines Agency… As the use of solvents is covered specifically under the medical products legislation with specific limits for specific substances referring to that guideline, we claim that 1,2-dichloroethane, (CAS 107-06-2) to be exempted from Authorisation) in the production and analytics of medicinal products (including the production of intermediates to manufacture medicinal products). In addition we request an exemption for associated PPORD activities for up to 10 tonnes/pa	
8	2012/09/18 15:18	Company Germany	We request an exemption for the filling of 1,2-dichloroethane into small packages for lab use. The use of 1,2-dichloroethane as analytical standard and for testing of residual solvents is exempted from authorisation as is the use as solvent in lab syntheses (scientific R&D). Competitors who could import the substance in small bottles for lab use and EU-manufacturers have a competitive advantage compared to companies just refilling a substance for low volume applications due to the fact that they do not need an authorisation. EU manufacturers as well as companies refilling 1,2-dichloroethane usually refill 1,2-dichloroethane from intermediate bulk container into small packages. An EU manufacturer could claim this step as part of the manufacturing process which is exempted from authorization requirements. Consumers are not exposed to 1,2-dichloroethane due to these uses. The substance is used as solvent for spectroscopy or liquid chromatography. These applications are routine analytical uses in laboratories within the scope of scientific R&D. The risk for the environment and consumers is very low. Usually the volume of the used substance is low. Additionally, the substance is classified as class 1 residual solvent in pharmaceutical synthesis ((EMA/CHMP/ICH/82260/2006 ICH Topic Q3C (R5) Impurities). Therefore, the use of 1,2-dichloroethane for testing of residual solvents should be exempted from authorisation (scientific R&D). The filling/packaging of 1,2-dichloroethane for scientific R&D purposes should be exempted from authorisation, too.	Thank you for your comment. If not generically exempted in the REACH Regulation, uses of a substance subject to authorisation can only be exempted from the authorisation requirement on the basis of Article 58(2) of REACH. Although uses for scientific research and development of a substance are exempted from the authorisation requirement in accordance with Article 56(3), this appears to only apply to its final use for SRD purposes under the conditions defined in Article 3(23). However, use of a CMR substance included in Annex XIV, on its own or in a mixture (above the lowest of the concentration limits specified in Directive 1999/45/EC or in Part 3 of Annex VI to Regulation (EC) No1272/2008), for e.g. re-filling or formulation with the intention to supply them for SRD purposes, would probably require authorisation. According to Article 58(2) REACH it is possible to exempt from the authorisation requirement uses or categories of uses *'(…) provided that, on the basis of the existing specific Community legislation imposing minimum requirements relating to the protection of human health or the environment for the use of the substance, the risk is properly controlled'.* This basis has not been provided here.

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
				As 1,2-dichloroethane is a carcinogen, there is a strong societal interest to protect humans, in particular workers handling the substance, from risks potentially arising from its uses. An authorisation requirement for 1,2-dichloroethane will accordingly ensure that the health of workers in the EU involved in the uses of this substance is protected. See also response to comment 1 in section I. Regarding the processes such as refilling performed by manufacturers of a substance, whether they are in the scope of authorisation or not is an issue for which ECHA has initiated discussions that are currently taking place in the European Commission. As soon as the issue has been clarified, ECHA will communicate the outcome in its website, e.g. at the Questions & Answers section (http://echa.europa.eu/web/guest/support/faq/questions-and-answers-on-applications-for-authorisation).
7	2012/09/18 14:45	EDC Downstream User Working Group Other contributor France	As (1) the use of EDC is covered specifically under the pharmaceutical legislation, (2) EDC is already under the scope of the Carcinogen directive (which is under revision - see IOM report) and (3) VOC directive applies to the use of EDC in fine and speciality chemistry, we claim EDC to be exempted from Authorisation. It is not the intention of REACH to impact market availability of health care products and phyto-pharmaceutical products that are adequately regulated through other European directives and regulations (REACH Recital 111)(please check the enclosed file for further explanations)	**Regarding exemption based on medicinal and veterinary regulations** See response to comment 1 in section I
6	2012/09/17 22:18	Company Ireland	The use(s) or categories of uses that are proposed to be exempted: Use of 1,2-dichloroethane as a solvent in the production of medicinal products under strictly controlled conditions. Community legislation, which is considered to justify the proposed exemption(s): Directive 2001/83/EC & Regulation (EC) No 726/2004 1999/13/EC Solvent Emissions Directive Article 5(2) of the 2004/37/EC Carcinogens and Mutagens Directive	**Regarding exemption based on medicinal and veterinary regulations** See response to comment 1 in section I

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			2000/76/EC Waste Incineration Directive PLEASE SEE ADDITIONAL COMMENTS IN SECTION IV	
5	2012/09/17 20:07	Company Sweden	The use of 1,2-Dichloroethane as process chemical (solvent) is vital for the manufacture of fine chemicals that are used by the Pharmaceutical and Biopharmaceutical industries to manufacture and purify Active Pharmaceutical Ingredients necessary in the development of medicinal products. The fine chemicals manufactured using 1,2-Dichloroethane as process chemical are not used and classified as medicinal products. There are currently no known technically equivalent substitutes for this use. As acknowledged by ECHA in the draft background document for 1,2-dichloroethane (June 2012), "the Annex XV report (2011) does not provide detailed information on alternatives to EDC for its use as a solvent. It is stated that industry is making efforts to substitute EDC, where possible. However, it might be difficult to develop alternatives for some specific applications, particularly in the pharmaceutical industry". In the light of this acknowledgement, the inability to use 1,2-Dichloroethane or introduce less hazardous alternatives in the manufacturing processes of the fine chemicals used by the Pharmaceutical and Biopharmaceutical industries will adversely impact the production of Active Pharmaceutical Ingredients and medicinal products. In addition, the use of 1,2-dichloroethane as an intermediate in fine chemical synthesis and as a solvent in chemical and pharmaceutical industries represents only around 0.2 % of the total used amounts. We therefore request ECHA's consideration to exempt from the authorization requirement the use of 1,2-Dichloroethane as process chemical (solvent) during the manufacture of fine chemicals used in the manufacture and purification of Active Pharmaceutical Ingredients. This exemption is necessary to avoid serious disruption to the manufacture of Active Pharmaceutical Ingredients and medicinal products by the Pharmaceutical and Biopharmaceutical industries and to ensure that innovation in the field of drug discovery in the European Union is allowed to continue.	**Regarding the request for exemption:** See response to comment 18 in section I
3	2012/09/17 18:32	Pharmachemical Ireland Industry or trade association Ireland	1,2-dichloroethane is used during the syntheses of active pharmaceutical ingredients as a solvent in a closed batch process,. Typically the handling, use and destruction of 1,2-dichloroethane at the use facility involves the following steps: • Transfer from road tanker to dedicated storage tank via contained piping, • Transfer from bulk storage tank to reaction vessel, via contained piping,	**Regarding exemption based on medicinal and veterinary regulations** See response to comment 1 in section I

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			• Periodic cleaning and maintenance works under strictly controlled conditions • Sampling via closed loop system, • Transfer of liquid waste stream from reaction vessels via contained piping to dedicated storage tanks, • Destruction of liquid waste stream by incineration as per an IPPC licence. Other risk management measures in place which have been in place prior to registration of this substance: • Substance is handled only by trained personnel • Substance handling procedures are well documented and strictly supervised by the site operations personnel. Additionally the manufacture of active pharmaceutical ingredients is performed within enclosed equipment in accordance with Good Manufacturing Practices (GMP). 1,2-dichloroethane (and other solvents) are introduced into the reactors via transfer systems designed to minimise environmental release, by trained personnel, and are thus contained within the process stream. In light of the above, exemption from authorisation is requested for the use of 1,2-dichloroethane in the production of medicinal products as defined in Art. 1(2) of the Directive 2001/83/EC relating to medicinal products for human use and in the production of veterinary products as defined in Art. 1(2) Directive 2001/82/EC for medicinal products for animal use, as outlined in REACH Art. 58(1)e. Mention the Community legislation which is considered to justify the proposed exemption(s) Directive 2001/83/EC & Regulation (EC) No 726/2004 1999/13/EC Solvent Emissions Directive 2004/37/EC Carcinogens and Mutagens Directive 2000/76/EC Waste Incineration Directive	
1	2012/09/11 15:31	Bayer HealthCare Company Germany	PROC3 Use in closed batch process (synthesis or formulation) PROC8b Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities. PROC15: Use as a laboratory reagent PPORD activities for up to 10 tonnes/pa	**See response to comment 1 in section I**

IV - Comments on uses for which review periods should be included in Annex XIV, including reasons for that: NONE