29 NOVEMBER 2012

Responses to Comments Document (RCOM) on ECHA's Draft 4th Recommendation for N,N-Dimethylacetamide (EC number: 204-826-4)

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_dmac_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
47	2012/09/19 22:21	ChemSec International NGO Sweden	We support the recommendation to include this substance in Annex XIV.	Thank you for your opinion.
46	2012/09/19 22:02 See attachment *46_Trade Union List.xls*	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 the information, and for providing your opinion.
45	2012/09/19 21:46	Company Portugal	1. - A few notes about FISIPE FISIPE is a Portuguese producer of acrylic fibres using DMAC in its process. Fisipe produces 50 000 - 55 000 ton of fibre per year (it depends of the productive mix). FISIPE exports, to third countries, around 75 % of its production - approx 80 M€/year in a total of 120 M€/year. FISIPE has developed special fibres. FISIPE is developing Precursor for Oxidized Fibres and Carbon Fibres. Within two year Fisipe will be a producer of Precursor for Oxidized Fibres and Carbon Fibres. Carbon Fibres are among the products that are considered strategic in EU and are integrated in the list of critical products for Space and Defence technologies. Fisipe is a partner in a project called EUCARBON, financed by 7th Framework Program of EU. EUCARBON project got an approval from the EU, because: "The projects are expected, first and foremost, to reduce the dependence on critical technologies and capabilities from outside Europe for future space applications, as identified in the EC-ESA-EDA Critical Space Technologies for European Strategic Non-Dependence - List of Urgent Actions 2010/2011."	Thank you for your comment and the provided information. As regards the information on risks associated to your use, alternatives and socioeconomic considerations please see response to comment # 41 in this section. In relation to the assessment of the wide-dispersiveness (# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in this section.

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			There is a marked dependence on the carbon fibre produced in USA and Japan. It is important for Europe to overcome this dependency. If in Europe are placed restrictions on the use of DMAC, the dependence will continue for many more years (most likely 8-10 years). A great player in the market for precursor carbon fibre is Mitsubishi. This company has the same production process that Fisipe. Aksa(Turkey) is another great player and it has the same process. The customers are demanding that the fibres produced by FISIPE have Oeko-Tex Standard 100 certification. The certification of FISIPE fibres is Class I, which means that the fibre can be used in baby clothing (the highest standard in safety). DMAC is the best or one of the best solvents used in the production of textile fibres and carbon fibre precursor. It is also the most widely used solvent. Another important aspect is that DMAC is the solvent that allows lower power consumption, which is an important environmental and economic aspect. 2. - About the use of DMAC 2.1. - The use of DMAC at acrylic fibre production Fisipe uses DMAC in dope suspension stage, in the spinning fibre stage and in the pigment preparation. The pigment preparation is used to inject into dope flow and produces pigmented fibres. DMAC is recovered in a solvent recovery area. In the case of fibres for textile use, DMAC levels are very low. In the particular case of fibre produced by FISIPE these values are residual. The average values of 2011 of DMAC content in the fibre is 0.11% - this means that DMAC is an impurity. 2.2. - DMAC and protection of the workers Fisipe controls its production process. Fisipe implemented appropriated procedures to protect the workers at the different places where DMAC is used, it monitors the work place and Fisipe's workers have training / education about DMAC risks and protection. Fisipe has an occupational health service that monitors the health of workers. 2.3. - DMAC and environmental protection According to Portuguese legislation and Environmental Permit, the DMAC releases are reported to the national authorities (air legislation, water legislation, IPPC Directive, E-PRTR, …).	

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			We can consider different kinds of DMAC releases: - to the waste water treatment; - to the air (emissions through the chimneys and fugitive emissions on some equipments) ; - in the wastes; - residual content in fibre. The solvent recovery facility has not walls (it is an open space). This means there is rapid dispersion of pollutants and that the exposure of workers has not meaning. 2.4. - Other Good Practices DMAC is used in industrial applications where there is a set of good practices implemented that ensure the safety and health of the workers. FISIPE is covered by the IPPC Directive (Integrated Pollution Prevention and Control). From this Directive arises the necessity of the company have an Environmental License issued by national authority. The operation of the facility is subject to the use of techniques identified as BAT (Best Available Techniques). These techniques were adopted by the European Commission as BREFs. The applicable BREFs are: - Reference Document on Best Available Techniques in the Large Volume Organic Chemical Industry - BREF LVOC; - Reference Document on Best Available Techniques in Common Waste Water and Waste gas treatment / Management Systems in Chemical Sector - BREF CWW; - Reference Document on Best Available Techniques in Emissions from storage - BREF ESB; - Reference Document on Best Available Techniques to Industrial Cooling Systems - BREF CV; - Reference Document on the General principles of Monitoring - BREF Mon; - Reference Document on Best Available Techniques in the Production of Polymers - BREF POL: The company has mechanisms to monitor the process of preparation and review of BREFs to ensure the adoption of BAT in its facilities. According to the Environmental Permit, BREFs are periodically re-examined to identify any BATs in these documents and with potential for implementation at the facility. 3. - DMAC in articles 3.1. - DMAC in fibre produced by Fisipe The fibre produced by is sold as of tow, staple and top and it can be	

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			grouped as: - Crude fibre; - Gel dyed fibre; - Pigmented fibre; - Fibres for technical applications. The average values of 2011 of DMAC content in the fibre is 0.11%. 3.2.- DMAC evaporation from the fibre Fisipe made some tests to measure the DMAC evaporation from the fibre to the air and we can conclude that, in normal use, there is no DMAC evaporation from the fibre to the air. The differences between different measurements are below the uncertainty of the measurement method. Given these data we can conclude that workers' exposure to DMAC evaporated from the fibre has no meaning. 3.3 - Conversion of acrylic fibre Fisipe sells its fibre for applications such as Knitting, Building Materials, Home Textiles, Fur Imitation, Tarps / Canvas, Blankets, Tires, Filters, Tricot, Nonwovens, Batteries, Protective Clothing, Roads, Automotive Industry, Tissues. For the above applications are carried out different types of operations: mechanical, thermal and chemicals. Fisipe made some measurements in articles resulting from different types of applications - for example, in applications of ecru fibre. The raw fibre is most fibre produced by Fisipe (57%). This type of fibre is subject to mechanical and dyeing operations (batch process). It was measured DMAC content in the articles obtained. In several samples the DMAC was not detectable and in others it was below to limit of quantification of the method. 4. - Effects of changing the solvent 4.1. - About the difficulty of changing the solvent There are different processes to produce acrylic fiber. Some processes use inorganic solvents (nitric acid) use other organic solvents (DMAC, DMF, sodium thiocyanate). However the processes are very different layouts and characteristics. This means that the change of the solvent implies large changes of equipment, control systems and buildings in key areas (recovery of the solvent, a dope preparation and spinning). In fact, the conversion of units of acrylic fibre production is technically difficult and very expensive. This means that large investments are needed. However, there is no case of solvent change in acrylic fibre producers	

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			Other consequence is that all development work of the last four years is compromised. It will be lost too some development work of precursors of very high module that is ongoing including the project EUROCARBON. Additionally it is not possible to predict the implications on the quality of fibre - chemical characteristics and physical characteristics (mechanical and softness of fibre touch). The new fibre may be poorly accepted by the market. In summary the change of solvent put great economic and financial problems to the company. The change may put into question the survival of Fisipe. 4.2 - About the business competition The above mentioned could lead to increased imports of acrylic fibre produced (in third countries) with processes using DMAC (Turkey, China and Japan). 4.3 - Socio economic issues The loss of competitiveness of Fisipe and its closure would have serious regional consequences with rising unemployment. Moreover, the uncertainty caused may compromise future investments. FISIPE invested in 2011 around 3 M€ including 1.5 M€ in R&D. FISIPE will invest in next following year more than 20 M€. FISIPE exports to third countries around 75 % of its production approx 80 M€/year in a total of over 120 M€/year. The activity of FISIPE creates around 340 direct jobs around 50 indirect jobs. In addition FISIPE contracts maintenance services of about 350 000 € / year of which nearly 80% is allocated to support costs of manpower (contractors).	
44	2012/09/19 18:44	European Trade Union Confederation European Trade Union Confederation Belgium	ETUC supports the inclusion of this substance in the Authorisation list. This substance is also included in the Trade Union Priority List for Reach authorisation. see: http://www.etuc.org/a/6023	Thank you for the information, and for providing your opinion.
43	2012/09/19 18:40	Dralon GmbH Company Germany	Dieser Kommentar zur Priorisierung von N,N-Dimethylacetamid beschreibt den Umgang mit dem Lösemittel innerhalb des Dralon-Werkes in Lingen/Deutschland. Er spezifiziert und unterstützt den Kommentar der CIRFS, European Man-made Fibres Association.	Thank you for your comment and the provided information.

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			Das Werk Lingen stellt Polyacrylfasern im Nassspinnverfahren her. Im Prozeß wird DMAc als Lösemittel für das Polyacryl-Pulver verwendet. Die Anlage in Lingen ist für eine Kapazität von ca. 70.000 t Polyacrylfaser jährlich ausgelegt. Die durchschnittliche Auslastung der letzten fünf Jahre liegt bei 60.000 t. Polyacrylfaser wird im globalisierten Markt vertrieben. Der Exportanteil (außerhalb EU) liegt bei ca. 80 %. Innerhalb der EU wird die Dralon L-Faser in u. a. Deutschland, Finnland, Litauen, Polen, Tschechische Republik, Österreich, Rumänien, Bulgarien, Mazedonien, Italien, Spanien, Frankreich und Belgien zur industriellen Weiterverarbeitung an Garnhersteller und Färbereien geliefert. N,N-Dimethylacetamid (im weiteren Text DMAc genannt) wird bei der Dralon GmbH seit über vier Jahrzehnten als Lösungsmittel in der Polyacrylfaserherstellung eingesetzt. Ständige Prozess- und Qualitätsoptimierungen haben die dralon L – Faser zu einer hochwertigen Chemiefaser reifen lassen. Kunden in aller Welt schätzen die dralon L-Faser wegen ihrer hervorragenden Eigenschaften. Die Verwendung von DMAc unterliegt seit ebenso langer Zeit, z. B. den Vorgaben aus dem Gefahrstoffrecht, dem Bundesimmissionsschutzgesetz und seinen Verordnungen, der TA Luft, dem Abfallrecht und dem Wasserhaushaltgesetz. Nicht nur diese rechtlichen Vorgaben, sondern vielmehr unsere Fürsorgepflicht gegenüber unseren Mitarbeitern, Kunden, Nachbarn und nicht zuletzt der Umwelt veranlasst uns hier zu verantwortungsvollen Handeln. Bei DMAc handelt es sich nach bisherigen Kenntnissen um einen CMR-Stoff der Kategorie 1 B. Schon lange vor dieser Einstufung wurden Maßnahmen vor, während und nach dem Umgang mit DMAc festgelegt um mögliche Gefährdungen für Mitarbeiter und nachgeschaltete Anwender auszuschließen. Die durch den Gesetzgeber vorgegebenen Arbeitsplatzgrenzwerte (AGW, TRGS 900)und Biologische Grenzwerte (BGW, TRGS 903) werden regelmäßig überwacht. Durch die vorhandenen Richtlinien und Gesetze auf nationaler und europäischer Ebene ist der Umgang mit DMAc lückenlos geregelt. Die	As regards information on the risks associated with your use and potential alternatives, please see response to comment # 41 in this section. In relation to the assessment of the wide-dispersiveness (# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in this section. In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in this section. (This response also considers the medicinal products legislation.)

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			Dralon GmbH hat u. a. mit den zuständigen nationalen Behörden ein umfassendes Monitoringprogramm für Umwelt und Arbeitssicherheit unter streng kontrollierten Bedingungen entwickelt und umgesetzt. Die fortlaufende Erfassung und Bewertung der Daten zeigt den verantwortungsvollen Umgang mit DMAc. Die bei dem Institut für Arbeitssicherheit der Deutschen gesetzlichen Unfallversicherung erhobenen Daten zur Erstellung von REACh-Expositionsszenarien für N, N-Dimethylacetamid in der Textilindustrie bestätigen, dass auch beim nachgeschalteten Anwender keine Gefährdung der Mitarbeiter vorliegt. Wir können diese Aussage bestätigen, nachdem wir einzelne Tätigkeiten der Anwender nachempfunden und mit Messungen belegt haben. Die bereits genannten Regelungen zum sicheren Umgang mit DMAc schützen die Umwelt und unsere Mitarbeiter umfassend. Ein Risiko für den nachgeschalteten Anwender und den Endverbraucher ist bei bestimmungsgemäßer Verwendung ausgeschlossen. Ein nicht ausreichend beherrschtes Risiko ist somit nicht vorhanden. Die rechtlichen Vorgaben, die im CIRFS Kommentar exakt beschrieben sind, sprechen unseres Erachtens gegen eine Eröffnung eines Zulassungsverfahrens nach Titel VII – Zulassung – der REACh-Verordnung 1907/2006, die in Artikel 55 eine Zulassung für die von besonders besorgniserregenden Stoffen ausgehenden Risiken, die nicht ausreichend beherrscht werden, fordert.	
42	2012/09/19 18:35	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 providing your opinion. As regards your comment related to whether authorisation is the most appropriate risk management option, please see response to comment #8 in this section. In relation to the assessment of the wide-dispersiveness (# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in this section.
41	2012/09/19	Federchimica	The substance has specific uses for which there is not potential	

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	17:10	Industry or trade association Italy	alternatives with a better profile and lower hazard profile (for example NMP has the same hazard profile of DMAC). It has used in very complex production chain such as automotive sector where to preview alternative in short time results impossible. In addition, on the economical side, must be have to consider the type of downstream users: it should be highlighted the effect that the change of any polymeric constituent or solvent inside formulations for automotive sector, as in this case, will entail the consequent re-homologation of the products of the whole industry. The modifications of enamels will overcome also the magnet wire manufacturers, up to reach the end user who in his turn will have to revalidate the products as required in the articulate quality procedure of the automotive division. It is highly probable that this process will have a big impact on the companies: the time needed to re-homologate the products of the whole automotive division, not only will slow down the business but will have also negative effects from the economic point of view. On the basis of the "Draft background document for N,NDimethylacetamide (DMAC)" of 20th June, it is also evident that the volume of DMAC used for "industrial coatings" is quite low because it's 3-5% of the total of the DMAC in the EU is used for "industrial coatings" (and so this specific case of enamels of magnet wire for the automotive division is also lower than the total percentage for "global" industrial coatings use) and so this specific case has a very low "contribution" to the total volume of DMAC, with the conclusion that impact of this use to the global risk of DMAC to human health and to the environment is very limited.	Thank you for your comment and the provided information. Topics such as the availability and suitability of alternatives and the need to get their use certified or approved, 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 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.
40	2012/09/19 16:24	Company	i) Aprotic solvents, such as DMAc should be exempted from the authorisation process because it has a defined safe level (threshold) when used in the industrial sector.	Thank you for your comment. As regards your proposal for restriction (for professional

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		Turkey	ii) The better option to manage any possible risks from DMAc is to use the Restriction process to control risk of non-industrial uses, by that route. It is considered that Authorisation is a disproportionate Risk Management Option. iii) ECHA's recommendation for prioritization of DMAc for authorisation considers an article as one major source for DMAc exposure and possible health risks for workers. Risks or substance exposure due to substance release from articles cannot be controlled by authorisation but must be regulated by a restriction. Consequently authorisation is an ineffective risk management option. iv) DMAc is used in the manufacturing process and small residues remain bound in the fibres. The REACH legislation requires that 'articles' (i.e solid objects, which fibres are considered to be under the REACH definition of article) that incorporate substances on the candidate list must be labelled accordingly. Fibre importers in Europe, have already expressed concern at this issue and have indicated they are considering switching to alternative materials. Despite no risk to workers or consumers having been shown, so far, purchasers are clearly reacting adversely to the situation. This is causing severe economic disadvantages.	and consumer uses) as an alternative risk management option to authorisation, please see response to comment #8 in this section. Please also note that exposure to potential residues of DMAC in produced articles is only one of the concerns associated with exposure resulting from the uses of DMAC, and not necessarily the primary one. See response to comment 21A in this section. In relation to thresholds, please see response to comment #31 in this section. As regards the socioeconomic considerations, please see response to comment #13 in this section. In addition, please note that the prioritisation approach which was agreed and applied here to prioritise and recommend substances from the Candidate List for inclusion in Annex XIV is not intended to assess the risks arising from the uses but to provide a very basic and general assessment of the use pattern and exposure potential a substance may have for humans (workers, consumers) or/and the environment. If a substance is included in Annex XIV it is then the obligation of the applicant for authorisation to demonstrate that the risks arising from the applied for uses are properly controlled or that there are no alternatives available and the socio economic benefits of the use outweigh its risks. Consider please also that beside proper control of risks substitution of SVHCs, where technically and economically viable, and good functioning of the internal market are objectives of the authorisation title.
38	2012/09/19 13:46	Individual	it should be highlighted the effect that the change of any polymeric constituent or solvent inside formulations for automotive sector, as in this	Thank you for your comment.

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		Italy	case, will entail the consequent re-homologation of the products of the whole industry. The modifications of enamels will overcome also the magnet wire manufacturers, up to reach the end user who in his turn will have to revalidate the products as required in the articulate quality procedure of the automotive division. It is highly probable that this process will have a big impact on the companies: the time needed to re-homologate the products of the whole automotive division, not only will slow down the business but will have also negative effects from the economic point of view.	Please see response to comment # 41 in this section.
37	2012/09/19 11:07	MSCA Sweden	We support the prioritisation of N,N-dimethylacetamide for inclusion in Annex XIV. The substance has high priority due to high volume and wide dispersive use.	Thank you for your opinion
36	2012/09/19 10:39	 Company France	This coumpond is used to manufacture pharmaceutical actives and for the present time, even if we have already tried to make substitution we have not yet succeed in it.	Thank you for your comment. Please see response to comment # 41 in this section.
33	2012/09/18 21:44	European Federation of Pharmaceutical Industries & Associations International organisation Switzerland	With ECHA's 4th recommendation published on 20th June 2012, the substance N,N-Dimethylacetamide (DMAC) 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 N,N-Dimethylacetamide (DMAC) in Annex XIV, including the prioritisation of the substance Within the Pharmaceutical Industry, DMAC is used both in lab R&D and in the supply chain of Active Pharmaceutical Ingredients (API's). For the production of pharmaceuticals, DMAC is one of a class of extremely useful solvents designated as polar aprotics to support reactions for producing intermediates and API's. Rates and selectivity of certain reactions (e.g. nucleophilic substitutions) are substantially enhanced due to the solvent polarity and other properties. Polar aprotic solvents such as DMAC are essential for these reactions, since they prevent unreacted materials from being carried forward in the process stream, they minimise the formation of side products, and produce intermediates and API's of the highest quality. In some cases, the properties of DMAC are unique in effecting a desired reaction reactivity, selectivity, solubility, or purification and no	Thank you for your comment. Please see also response to comment # 41 in this section. **<u>Article 2(5) exemption response</u>** 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. **<u>Article 58(2) exemption response</u>** 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

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			comparable performance with any other solvent is known or the alternative solvents pose a greater environmental, occupational health, or other concern. There are other polar aprotic solvents with similar physical or chemical properties (albeit of lower polarity) that could potentially be used in place of DMAC in some API manufacturing syntheses. The most common 'direct' alternative may be DMF (N,N-dimethylformamide). Others include formamide, N-methylformamide, N-methyl pyrrolidon and N-methylacetamide. However, these alternatives carry essentially the same health hazard as DMAC. Some of these solvents are already on the REACh Candidate List. In addition, these solvents have lower polarity and for some purposes different reactivity; the replacement of DMAC with such solvents could lead to incomplete reactions and side products that impact the safety and quality of the API. Moreover, this would result in an increase in waste streams. The manufacture of APIs and associated intermediates are performed in enclosed reactor trains in accordance with Good Manufacturing Practices (GMP). DMAC (and other solvents) are introduced into the reactors via transfer systems designed to minimize environmental release, by trained personnel using appropriate engineering controls and/or protective equipment, and are thus contained within the process stream. Occupational exposure is also controlled through compliance with the Chemical Agents Directive (98/24/EC). Since the residual amount of DMAC in the eventual product (drug substance) is safety-limited by the ICH Q3C (Guideline for Residual Solvents), in practice virtually all the DMAC used during manufacture would be present in the waste streams that are disposed in accordance with local environmental regulations. Thus, the risks of environmental exposure of DMAC in the pharmaceutical manufacturing environment are minimized by the equipment design and operational controls; disposal and record-keeping procedures exist within the governance of the quality system.	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 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[1] 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

[1] 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.

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			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 N,N-Dimethylacetamide, (CAS 127-19-5) 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	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 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 N,N-Dimethylacetamide. Therefore, they may be not regarded as a sufficient basis for exempting uses of N,N-Dimethylacetamide from authorisation in accordance with Article 58(2) of the REACH Regulation. Council Directive 98/24/EC on the protection of the health and safety of workers from the risks related to chemical agents at work (CAD) sets out a framework

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				based on the determination and assessment of risk and general principles for the prevention of risk, associated with hazardous chemical agents. CAD (through Directive 2000/39/EC) establishes indicative occupational exposure limit values for DMAC. In addition, CAD 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 CAD imposes binding minimum requirements for controlling risks to human health. Therefore, CAD may not be regarded as a sufficient basis for exempting uses of N,N-Dimethylacetamide from authorisation in accordance with Article 58(2) REACH Regulation. **PPORD exemption request** As relates to your request for exemption for PPORD, please see response to comment #10 in section III of this document.
32	2012/09/18 18:45	Company Spain	Montefibre Hispania S.A. would like to support and document the comments made by CIRFS on behalf of the European Man-made fibers industry. In particular we would like to comment the information given in the draft recommendation about the use of DMAc in man-made fibers industry and the ECHA document supporting prioritization for the inclusion of DMAc in Annex XV. The use of DMAc at Montefibre Hispania for our acrylic fiber production is an adequately controlled industrial use. The use is very well regulated by existing legislation and production permits and our industrial activity is regularly controlled by the competent authorities. Potential risks related to DMAc dermal absorption and inhalation are considered to be low and	Thank you for your comment and the provided information. As regards your proposal for restriction (for professional and consumer uses) as an alternative risk management option to authorisation, please see response to comment #8 in this section. As regards information on the risks associated with your use and potential alternatives, please see response to comment # 41 in this section.

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			appropriately managed by Montefibre Hispania Health and Safety management system. Rigid risk management measures are implemented across the production process to protect the operators at the different stages of the process and under all working conditions (normal, start/stop, maintenance, cleaning...). These measures range from workplace DMAc measurements and biomonitoring checked against the no effect levels on health-DNEL to basic training on how to work safely. Montefibre Hispania also has and efficient environmental management system implemented and all liquid and solid effluents as well as solid residues are managed according to current legislation and to the limits established in Montefibre Hispania´s Integrated Environmental Authorization. Detailed information about DMAc industrial use and management in Montefibre Hispania facilities is provided as a confidential document in order to comply with EU competition law. Montefibre Hispania acrylic fibers do not contain 3% residual solvent as stated on page 4 of the draft recommendation. Residual DMAc in fiber will depend on the type of fiber but is significantly lower than this value. Lab scale dermal absorption and inhalation exposure simulation tests do not reveal any risks for our downstream users(see section 6 confidential document).. Regarding to the ECHA document supporting prioritization of DMAc for inclusion in Annex XV, Montefibre Hispania would like to emphasise that there is no use of DMAc in the fiber and it is only present as a production impurity. In the ECHA document the sites involved in the use of DMAc are identified as follows: fiber production 1-10, fiber processing 100-1000, textiles production>1000. Consequently, since there is no use of DMAc in our article only the fiber production sites (6 fiber manufacturers in the EU) should be considered for the score. Based on these statements and all the information provided in the confidential report, Montefibre Hispania considers that there is an adequate control and protection of the workers in our production plant and that if the i-OEL is met, there is no health risk. This argumentation should lead to an exemption for the use of DMAC at industrial scale operations where i-OEL is respected.	In relation to the assessment of the wide-dispersiveness (# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in this section. **Art 58(2) exemption response** In regard to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in this section. This response also considers the Chemical Agents Directive.

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			If the exemption is not considered, Montefibre Hispania believes that a restriction focused on the non-industrial uses (i.e. professional and consumer) will be a much better risk management option than authorisation.	
31	2012/09/18 18:18	Company Switzerland	N,N-dimethylacetamide (DMAC) is used by industry as a solvent in cases where other solvents are not appropriate because of their intrinsic properties. DMAC is a dipolar, aprotic solvent with high solving power and its high boiling point allows reactions to be carried out at higher temperatures. Therefore DMAC cannot easily be replaced by another solvent that is not on the candidate list. Very often it is possible to recycle DMAC and in any case it can be separated efficiently from the synthesized product. Finally the used DMAC will be treated as waste. Although DMAC cannot be considered to fall under the definition of a transported isolated intermediate within the frame of REACH Article 18(4) as it is not transformed into another substance itself, the handling within industry will be similar to the use of a transported isolated intermediate as described in REACH Article 18 (4). There are DNEL and PNECs known for DMAC and therefore industry will in any case aim to use procedural and control technologies that minimise emission and any resulting exposure. For any exposure scenario the exposure will be well below DNEL or PNEC. As a consequence the demands of REACH Article 60 (2) will be fulfilled at any time. Therefore we suggest not to include DMAC in REACH Annex XIV or alternatively to exempt uses at industrial sites where the risk to human health or the environment is adequately controlled, because of already known DNEL, PNEC that are relevant for the handling of DMAC within industry.	Thank you for your comment. **Low level of risk and lack of alternatives** As regards the information on risks associated with your use and on alternatives, please see response to comment # 41 in this section. **DNEL and PNEC available** Please further note that a threshold mode of action of a substance does not demonstrate as such that the associated risks arising from the uses of the substance are adequately controlled. Instead, it means that if an applicant is able to demonstrate in his application for authorisation adequate control of risks arising from the applied for uses on the basis of established effects thresholds and his exposure assessment he may be granted an authorisation (authorisation may also be granted if the applicant can demonstrate that there is no suitable alternative to the substance available and that the socio economic benefits of the uses applied for outweigh the associated risks for health and environment).
30	2012/09/18 17:07	Company United Kingdom	Within the Pharmaceutical Industry, DMAC is used both in lab R&D and in the supply chain of Active Pharmaceutical Ingredients (API's). For the production of pharmaceuticals, DMAC is one of a class of extremely useful solvents designated as polar aprotics to support reactions for producing intermediates and API's. Rates and selectivity of certain reactions (e.g. nucleophilic substitutions) are substantially enhanced due to the solvent polarity and other properties. Polar aprotic solvents such as DMAC are essential for these reactions, since they prevent unreacted materials from being carried forward in the process stream, they minimise the formation	Thank you for your comment. As regards the information on risks associated to your uses, on alternatives and socioeconomic considerations, please see response to comment # 41 in this section. Please see also response to comment #4 in this section. In relation to the assessment of the wide-dispersiveness

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			of side products, and produce intermediates and API's of the highest quality. In some cases, the properties of DMAC are unique in effecting a desired reaction reactivity, selectivity, solubility, or purification and no comparable performance with any other solvent is known or the alternative solvents pose a greater environmental, occupational health, or other concern. There are other polar aprotic solvents with similar physical or chemical properties (albeit of lower polarity) that could potentially be used in place of DMAC in some API manufacturing syntheses. The most common 'direct' alternative may be DMF (N,N-dimethylformamide). Others include formamide, N-methylformamide, N-methyl pyrrolidon and N-methylacetamide. However, these alternatives carry essentially the same health hazard as DMAC. Some of these solvents are already on the REACh Candidate List. In addition, these solvents have lower polarity and for some purposes different reactivity; the replacement of DMAC with such solvents could lead to incomplete reactions and side products that impact the safety and quality of the API. Moreover, this would result in an increase in waste streams. The manufacture of APIs and associated intermediates are performed in enclosed reactor trains in accordance with Good Manufacturing Practices (GMP). DMAC (and other solvents) are introduced into the reactors via transfer systems designed to minimize environmental release, by trained personnel using appropriate engineering controls and/or protective equipment, and are thus contained within the process stream. Occupational exposure is also controlled through compliance with the Chemical Agents Directive (98/24/EC). Since the residual amount of DMAC in the eventual product (drug substance) is safety-limited by the ICH Q3C (Guideline for Residual Solvents), in practice virtually all the DMAC used during manufacture would be present in the waste streams that are disposed in accordance with local environmental regulations. Thus, the risks of environmental exposure of DMAC in the pharmaceutical manufacturing environment are minimized by the equipment design and operational controls; disposal and record-keeping procedures exist within the governance of the quality system.	(# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in this section. **Article 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation that is not generically exempted from the authorisation requirement on the basis of REACH Articles 2(5 and 8) or 56(3, 4 and 5), please see response to comment #33 in this section. This response also considers the medicinal products legislation and the Chemical Agents Directive.
29	2012/09/18 16:45	Association of the British	Background	Thank you for your comment.

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
		Pharmaceutical Industry Industry or trade association United Kingdom	With ECHA's 4th recommendation published on 20th June 2012, the substance N,N-Dimethylacetamide (DMAC) 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 N,N-Dimethylacetamide (DMAC) in Annex XIV, including the prioritisation of the substance Within the Pharmaceutical Industry, DMAC is used both in lab R&D and in the supply chain of Active Pharmaceutical Ingredients (API's). For the production of pharmaceuticals, DMAC is one of a class of extremely useful solvents designated as polar aprotics to support reactions for producing intermediates and API's. Rates and selectivity of certain reactions (e.g. nucleophilic substitutions) are substantially enhanced due to the solvent polarity and other properties. Polar aprotic solvents such as DMAC are essential for these reactions, since they prevent unreacted materials from being carried forward in the process stream, they minimise the formation of side products, and produce intermediates and API's of the highest quality. In some cases, the properties of DMAC are unique in effecting a desired reaction reactivity, selectivity, solubility, or purification and no comparable performance with any other solvent is known or the alternative solvents pose a greater environmental, occupational health, or other concern. There are other polar aprotic solvents with similar physical or chemical properties (albeit of lower polarity) that could potentially be used in place of DMAC in some API manufacturing syntheses. The most common 'direct' alternative may be DMF (N,N-dimethylformamide). Others include formamide, N-methylformamide, N-methyl pyrrolidon and N-methylacetamide. However, these alternatives carry essentially the same health hazard as DMAC. Some of these solvents are already on the REACh Candidate List. In addition, these solvents have lower polarity and for some purposes different reactivity; the replacement of DMAC with such solvents could lead to incomplete reactions and side products that impact the safety and quality of the API. Moreover, this would result in an increase in waste streams. The manufacture of APIs and associated intermediates are performed in	Please see response to comment #30 in this section.

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			enclosed reactor trains in accordance with Good Manufacturing Practices (GMP). DMAC (and other solvents) are introduced into the reactors via transfer systems designed to minimize environmental release, by trained personnel using appropriate engineering controls and/or protective equipment, and are thus contained within the process stream. Occupational exposure is also controlled through compliance with the Chemical Agents Directive (98/24/EC). Since the residual amount of DMAC in the eventual product (drug substance) is safety-limited by the ICH Q3C (Guideline for Residual Solvents), in practice virtually all the DMAC used during manufacture would be present in the waste streams that are disposed in accordance with local environmental regulations. Thus, the risks of environmental exposure of DMAC in the pharmaceutical manufacturing environment are minimized by the equipment design and operational controls; disposal and record-keeping procedures exist within the governance of the quality system.	
28	2012/09/18 16:10	AK-KIM KIMYA SAN. VE TIC.A.S. Company Turkey	1) The European customers of Ak-Sa, which is our sister company and customer of our product DMAC have expressed their concern regarding residues of DMac held within the fibre. The potential public elevation of DMac to the status of 'substance of very high concern', is affecting sales of man-made fibres to EU customers. Despite no risk to workers or consumers having been shown, so far, purchasers of our Turkish customer AK-SA are clearly reacting adversely to the situation. This is causing severe economic disadvantages for us in regards to our sales in Turkey. 2) As our European agent, the biggest importer of DMAC is selling our product to European Fiber producer as well, the above impact is shown here as well, because they are selling their fibers to the same potential customer. This is a double disadvantage for our production. As a non-european producer we are clearly put in a disadvantaged situation here by a European legislation, which is not the aim of the whole	Thank you for your comment. Identification of the substance as SVHC and the subsequent prioritisation to recommend it for inclusion in Annex XIV is based on provisions laid down in the REACH Regulation. Please note that REACH is an EU Regulation aiming to ensure a high level of protection of human health and the environment while enhancing competitiveness and innovation. As DMAC is toxic for reproduction, there is a strong societal interest to protect humans from risks potentially arising from its uses. Subjecting the substance to the authorisation requirement will contribute to ensure that the health of workers in the EU involved in the uses of this substance is protected while the substance will be progressively replaced by suitable alternatives where economically and technically viable, Although subjecting DMAC to authorisation may have an impact on your company in its capacity as manufacturer

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			REACH legislation. This is a market effecting process, that should not be caused by REACH. …/2 3) Even as a non-european producer we will be forced to assist our representative in those markets, where they have traditionally sold our product both financially and with know-how to support the users in the authorization process. This will incur additional expense with the potential effect on competitiveness of the product. 4) This triple economic impact for our sales both on the domestic market as well as on the European market will cause redundancy to many workers and has an effect on the Turkish economy in the long term.	of DMAC, you are not disadvantaged by this measure as it has the same impact on all other manufacturers/suppliers of the substance to the EU market, no matter whether they are located outside or inside the EU.
27	2012/09/18 15:59	Company United Kingdom	We are referring to the comments submitted by CIRFS (EU Man-made Fibre Industry Association) to which we have given input and support. In order to complement these comments we have attached our additional confidential comments to this form below.	Thank you for your comment and the provided information. As regards your proposal for restriction (for professional and consumer uses) as an alternative risk management option to authorisation, please see response to comment #8 in this section. As regards information on the risks associated with your use, potential alternatives, and socioeconomic considerations, please see response to comment # 41 in this section. In relation to the assessment of the wide-dispersiveness (# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in this section and also the (updated) background document. **Art 58(2) exemption response** In relation to the elements ECHA considers when

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
				deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in this section. This response also considers the Chemical Agents Directive (and the medicinal products legislation).
25	2012/09/18 15:12 See attachment *25_2012 09 19_CIRFS comment.pdf*	CIRFS: European Man-made Fibres Association Industry or trade association Belgium	CIRFS general comment to the draft recommendation to list DMAC under Annex XIV (authorization) - CIRFS: European Man-made Fibres Association is convinced that Directive 2000/39/EU, establishing an indicative occupational exposure limit value (i-OEL) for DMAC, is Community legislation which provides the requirements for the proper control of the risks and for the protection of human health and for the environment. The implementation of i-OEL at Member States, remains over the whole process under the control of the European Commission. In the case of DMAC, having an i-OEL with skin notation, this has resulted in adequate control and protection (including adequate skin protection) of the workers at industrial operations. This includes MMF (man-made fibres) industry as being regulated, from chemical risks at Community level. If the i-OEL is met, there is no health risk. Above argumentation and motivation should lead to an exemption for the use of DMAC at MMF production locations and not to a recommendation for authorization. - Authorization is disproportionate and is a competitive distortion for EU industry The use at MMF industry is not wide-dispersive and the prioritization "score" is too high. There is no other use of DMAC than at MMF production. Thereafter, DMAC is a residual impurity in the fibre, embedded in the polymer, which is later significantly reduced by the intense washing and dyeing processes at converters and treated according to environmental permits. Potential risk related to airborne DMAC emissions from some fibre types is considered to be low and appropriately manageable by air management at the converting operations. The converters of the fibre receive data sheets on product safety, referring to the presence of DMAC as a residue and the	Thank you for your comment the provided information. Regarding your comment on the volumes for the acrylic and other man-made fibres, as well as the volume of DMAC used in those applications, please note that the figures in the *background document* had taken into account the information you had provided in your previous comment (made during the public consultation on identification of the substance as SVHC), and are therefore in accordance with that information. In relation to the assessment of the wide-dispersiveness (# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in this section and also the (updated) background document. As regards your proposal for restriction (for professional and consumer uses) as an alternative risk management option to authorisation, please see response to comment #8 in this section. Please see also response to comment #13 in this section. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in this section. This response also considers the Chemical Agents Directive (and the

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			measures that have to be taken during converting. Measurements within many areas of the fibre converting industry, done by IFA; the German Institute for Occupational Safety and Health of the German Social Accident Insurance over the years 2000-2011 have shown that over that decade, not a single measurement was above the established MAK (maximum workplace concentration), which is the same level as the i-OELV, with a vast majority of the results even being below the limit of quantification of 0.3 mg/m3. Also the OECD report, on page 9 and 11, says that there is no risk, and that the i-OEL is met at converter and end-user level. Taking above into consideration - safe use at MMF, no use further down the value chain and proven to be no risk- the recommendation to include DMAC in Annex XIV, which means applying for authorisation and granted only for a limited period of time, results in a strong market distortion with the non-European MMF producers, because of the huge uncertainty that it creates for the customers of European producers. In CIRFS view, the main gain from a health point of view, which is the main goal of REACH, will not be achieved by highly prioritizing DMAC for authorization. The high score for prioritization is not justified for MMF production, and very likely not by other industrial sectors. If the exemption is not accepted (see above), which in our view seems unjustified, authorisation would be disproportionate for MMF production and not be the right risk management option. Taking the above arguments into consideration as to MMF, a targeted restriction of the non-industrial uses; professional and consumer use, would result in a much better and more efficient management of risk.	medicinal products legislation.)
24	2012/09/18 15:02	DINOX Handels-GmbH Company Germany	1. For the draft background document for N,N-Dimethylacetamide (DMAC), dd. 20 June 2012 a) Aprotic solvents, such as DMac should be exempted from the authorisation process under the provisions of Art. 58.2 [on the basis that existing legislation already imposes minimum requirements relating to the protection of human health or the environment for the use of the substance]. DMac has a defined safe level (threshold). b) AUTHORISATION IS NOT THE MOST APPROPRIATE OR EFFICIENT	Thank you for your comment. As regards your proposal for restriction (for professional and consumer uses / uses of articles) as an alternative risk management option to authorisation, please see response to comment #8 in this section. Please also note that potential exposure to residues of DMAC in produced articles is only one of the concerns associated with exposure to DMAC, and not necessarily the primary one. Similarly, potential professional / consumer uses of articles containing DMAC do not

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			PROCESS TO MANAGE THE MAJOR SOURCES OF RISK IN THE USE OF DMAC. The majority of DMAC is used in industrial situations under controlled conditions posing no health risk to workers. c) THE BETTER OPTION TO MANAGE ANY POSSIBLE RISKS FROM DMAC IS TO USE THE RESTRICTION process to control risk of non-industrial uses, by that route. IT IS CONSIDERED THAT AUTHORISATION IS A DISPROPORTIONATE RISK MANAGEMENT OPTION. d) ECHA's recommendation for prioritization of DMAC for authorisation considers an article as one major source for DMAC exposure and possible health risks for workers. Risks or substance exposure due to substance release from articles cannot be controlled by authorisation but must be regulated by a restriction. CONSEQUENTLY AUTHORISATION IS AN INEFFECTIVE RISK MANAGEMENT OPTION. e) The majority of DMAC imported by us is already covered by other European legislations (Pharma, Biocide). This industrial uses as well as the fibre uses are all strictly controlled uses. f) Too great an emphasis has been made of the minor uses. The whole process is based on the minority uses. This is absolutely inappropriate. WE SUPPORT THE RESTRICTION OF THE MINOR USES AND THE EXEMPTION OF ALL INDUSTRIAL USES. 2. We would like to repeat our comments on Annex XV dossier for identification of a substance as SVHC, for which ECHA responded: "Provided that the substance will be identified as SVHC, this information may, where relevant, be considered at later stages of the risk management." QUOTE	necessarily constitute the major concern for DMAC and are not the reason for prioritisation of the substance, as there are other industrial uses identified with a high potential for occupational exposure. See response to comment 21A in this section. As regards your comment which had been submitted on Annex XV dossier for identification of a substance as SVHC, we note that this had been taken into account when assessing the priority of the substance and in the development of the background document for DMAC. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in this section. This response also considers the medicinal products legislation and the Chemical Agents Directive. Article 56(4)(b) REACH states that paragraphs 1 and 2 (the requirement to have an authorisation) '(…)shall not apply to the following uses of substances: (…) uses in biocidal products within the scope of Directive 98/8/EC'. Directive 98/8/EC and the Regulation (EU) 528/2012 (Biocidal Product Regulation, which will repeal Directive 98/8/EC from 1 September 2013) include a risk assessment and authorisation procedure for active substances and products containing these substances. N,N-Dimethylacetamide does not seem to be either approved as a new active substance and included in Annex I to Directive 98/8, or included in the review programme under the Biocidal Product Regulation. To qualify for the authorisation exemption for a biocide use, such use would need to be permitted. Therefore, there can be no exemption from authorisation based on "uses in biocidal products within the scope of Directive 98/8/EC".

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			Page 14, 30 The sentence „The fibers produced contain residual amounts of DMAC of up to 3%, which is released by the subsequent processing steps.“ in the summary is on its own misleading. The information from page 30 of the dossier “The residual content of DMAC in the final textile product is reported to be below detection limit.” should be added to this summary, to give detailed information. Page 16, 66 “DMSO is specifically marketed as alternative to DMAC.” To our knowledge DMSO is not a general alternative to DMAC, because due to its intrinsic properties it cannot replace DMAC for all uses. Page 19, 45, 55 The comment on page 19, 45 and 55: “…These limits were set to prevent the development of respiratory irritation in workers and do not take account of reproductive toxicity.(Scientific Committee on Occupational Exposure Limits, 1994) is not correct. The original text states: “if these limits are kept and not exceeded, no reproductive effects are to occur.” The effect of the respiratory system will start at much lower levels than the reprotoxicity effects, therefore the given IOELVs for the respiratory system will eliminate the possibility of reprotoxic effects automatically. Page 21-23, 25, 30, 42 The production volumes mentioned in the dossier regarding acrylic fibers seem to be too high. According to our knowledge these figures should be much lower. The total DMAC which is used for all fibers is estimated to be approx. 2.500 t. Therefore, the use for fiber production is considerably lower than the 25-30 % which are mentioned in the dossier. Page 22, 32, 44, 50 The use named “excipient (carrier ingredient) in human and veterinary pharmaceuticals” is not to be included in this dossier, because this is to be discussed in the pharmaceutical regulations. Addressing the matter in the pharmaceutical regulation will have more effect. Page 54, 55, 24-30	It needs to be examined whether an exemption can be granted under Article 58(2) REACH. The biocidal 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 N,N-Dimethylacetamide. Therefore, this legislation may not be regarded as a sufficient basis for exempting this use of N,N-Dimethylacetamide from authorisation in accordance with Article 58(2) of the REACH Regulation.

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			No DMAC is brought into the environment by waste disposal due to authorized waste processing systems. DMAC in fiber < 0,6 % - 0,1 % is possible Converters < 0,6 % Clothing manufacturers < 0,1 % Consumer below detection limit Page 59 Alternative DMSO Due to different reasons, we do consider DMSO not as a general substitute for DMAC: a) In the fiber production it is not suitable, as intrinsic properties will cause problems with the operational conditions (melting point), will cause concern due to decomposition products, that will form when the fiber is dried by heat evaporation (boiling point), which are hard to wash off and it causes garlic odour. Furthermore, there is no to only negligible consumer exposure via fibers. b) It is assumed, that DMSO is already used wherever possible due to the regulations being of advantage for DMSO. c) DMSO could be a substitute for paint strippers and solvent cleansers. Page 60 Alternative DMI We see two reasons for not considering DMI as a suitable substitute for DMAC. The first is due to no experimental data being available while the structural similarity alerts the concern for reproduction toxicology, especially for the fertility and maybe even developmental effects. The second reason is the missing biodegradability of DMI. With 90 % of the DMAC release is via the fiber industry, this will raise a persistence issue. Page 58 Alternative DMF, NMP In our opinion, this substance should not be in the dossier as possible substitutes, as they are both CMR 1a/b-classified and therefore not a suitable substitute. Page 58 Alternative NEP This product is expected to be classified CMR 1 a/b at a not so far point in time and is therefore not suitable as a substitute.	

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			Page 62 Alternative processes For high performance fibers the alternative of wet spinning is not suitable due to the loss of strength and thickness of the fiber. Wet spinning – is not really an alternative for DMAC, as this process is using DAMC as well. However, by intensifying the drying process of the raw yarn directly after the spinning, either in time or temperature, the DMAC-content could be reduced at the start. As raw yarn is being produced by well-equipped manufacturers, this would lead to a reduction of the environmental release at the source, that would be efficient. Page 62 Alternative process – Wet spinning Our sister company, the biggest acrylic fiber producer of the world, situated in Turkey has declared, that they are willing to improve their wet spinning process by increasing the washing time in order to have a bigger cleaning effect of DMAC without reducing the speed of production and by doing so, the final fiber will have a DMAC-content much lower than 0,1 %. This fibers are also being imported into the EU. Additional comment: The consortium registration dossier will be up dated in order to make sure to have ink eraser marked as a "not supported use".	
23	2012/09/18 14:48	Merck Sharpe & Dohme / Organon NV Company Netherlands	Exemption from authorization is requested for the use of N,N-Dimethylacetamide (CAS 127-19-5) in the production of medicinal products as defined in Art.1, (23) of the Directive 2001/83/EC relating to medicinal products for human use and Directive 2001/82/EC for medicinal products for animal use, in accordance with the process outlined in REACH Art. 58(1)e. The rationale for the request is based on the fact that the risks of using DMAC are properly controlled by existing Community regulation, in line with REACH Art. 58(2).	Please see response to same comment in section III of this document. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in this section. This response also considers the medicinal products legislation.
22	2012/09/18 14:10	Individual Germany	DMAc is an important solvent required in the industrial production of high-tech membranes, even when only used in small quantities and by few specialized membrane manufacturers in Europe. High-tech membranes are used for numerous highly specialized	Thank you for your comment and the provided information. As regards your comment related to whether

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			applications and thus contribute to the protection of health, environment and natural resources: production or purification of potable water, process water, food etc. None of these applications would tolerate hazardous residues of DMAc or other process solvents in the used membranes, as this would be in conflict to their intended use. The process solvent is an essential component of the membrane production technology. Substitution of a used solvent, like DMAc, is technically and chemically limited. The situation is not all comparable with applications like paint strippers. ECHA already mentioned the lack of alternatives for DMAc in its dossiers. Production sites in Europe already fulfil highest standards worldwide regarding protection of workers and the environment. Numerous national and European laws regulate environmental protection and health and safety at work in detail, especially use of dangerous substances like DMAc. Compliance is checked by local authorities and the Accident Prevention & Insurance Associations. So regarding these industrial applications of DMAc ECHA's proposal to prioritize DMAc is not justifiable. The authorization requirement for DMAc would only be additional red tape.	authorisation is the most appropriate risk management option, please see also response to comment #8 in this section. As regards information on the risks associated with your use, potential alternatives, and socioeconomic considerations, please see response to comment # 41 in this section. Please see also response to comment #4 in this section. In relation to the assessment of the wide-dispersiveness (# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in this section.
21 A	2012/09/18 12:42 See attachment *21a_BASF non-confidential comment.pdf*	BASF SE	Please refer to the attachment(s)...	Thank you for your comments. As regards your comment related to whether authorisation is the most appropriate risk management option, please see response to comment #8 in this section. Regarding the proportionality of an authorisation requirement, please see response to comment # 13 in this section. As regards information on the risks associated with specific uses, potential alternatives, and socioeconomic considerations, please see also response to comment # 41 in this section.

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
				<u>Priority assessment</u> **<u>- Assessment of volumes</u>** In the comment it is claimed that the "Volume" score should be decreased from 9 to 7 or even 5, with the justification that the main use (synthesis of agrochemicals, active pharmaceutical ingredients and fine chemicals, 65-70%) should be exempted based on Art. 58(2) and the second major use (production of man-made fibres, 20-25%) occurs under controlled conditions. It is noted that according to the agreed prioritisation approach, for the assessment of the "volume" criterion the complete annual volume supplied in the EU to uses not exempted from the authorisation requirement is taken as basis. The overall potential for exposure of the uses of the substance is instead considered in the assessment of the "wide dispersiveness" criterion – see paragraphs below. Further, after assessment by ECHA of the arguments brought forward by the commenting parties in relation to exemption requests under Article 58(2), it has been concluded that there seems to be no sufficient basis for exempting uses of DMAC from authorisation (see exemption-related responses below and to other comments). In conclusion, there seem not to be grounds for changing the assessment of volume covered by the authorisation requirement. **<u>- Assessment of wide-dispersiveness (# sites and potential for releases)</u>** **<u># sites</u>**

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				A number of comments submitted by industry suggest that the "site" score should be 2 instead of 3, because for production of fibres DMAC is used only at 6 sites, and it is assumed that on the basis of data submitted in this consultation the overall number of sites also for the other (main) industrial applications will be limited. It has been further requested to disregard sites at which articles (mainly fibres) containing DMAC impurities are used when counting the number of use sites in the EU, as such uses are not in the scope of authorisation. Here it should be noted that, according to the general prioritisation approach, the "total number of sites where the substance is used in the scope of authorisation" has to be considered. In this context, uses need to be considered in a lifecycle perspective when exposure resulting from use of articles containing a substance cannot be excluded). ECHA had calculated the original "sites" score on the basis of data and best-knowledge estimations, which are set out in the background document. In the current consultation, exact figures provided by some industry associations (see comments by CIRFS - #20 in section III; and EUROPACABLE - #25 in section I) agree with the non-confidential site ranges provided in the background document. Several companies provided also information on the use of DMAC in the production of polymeric films (e.g. dialyzer membranes), which had not been confirmed before, mentioning that this use occurs at <10 sites in the EU (see e.g. comment #4 in section I). Furthermore, some of the suppliers of DMAC submitted comments in which they claim that, based e.g. on the numbers of their customers, the overall number of industrial sites should be limited. Taking into account the information that already has been available (submitted in response to the consultation

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				performed during preparation of the Annex XV Dossier, during the consultation on SVHC identification of the substance, and in the registrations) and the new information submitted in this consultation on the site numbers, ECHA does not find sufficient grounds to change the assessment of wide dispersiveness of the use (see also updated background document – section 2.2.2.3). **potential for release** It should be noted that the prioritisation step in the authorisation process comprises a general evaluation of the use pattern and exposure potential a substance may have (mainly for workers and consumers in the case of CMR). The inclusion in Annex XIV is per substance and not per use (or installation). Therefore screening of release potential in the prioritisation phase does not assess the exposure levels from single uses (at specific sites), but aims to deduce whether there are uses/situations where potential for exposure cannot be excluded. ECHA had assessed that there are identified uses of DMAC which have a potential for significant occupational exposure. In particular, potential for exposure cannot be excluded during operations such as mixing and blending of DMAC in batch formulation processes where workers may have contact with DMAC; or during not enclosed or partially enclosed operations during uses such as fibre spinning or applying coatings by spraying / roller / brushing / pouring / dipping. A further concern is potential exposure of industrial or in some cases professional workers to residues of DMAC in fibres or in polyimide films. Quite many comments on the low risks associated with the above mentioned uses and processes have been provided by industry (see e.g. also comments # 16, 39,

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				which refer to several of the above processes; # 12 and 20 referring in particular to coatings; and # 25, 27, 32, 43, 45, which refer in particular to man-made fibres). It needs however be considered that DMAC is used at many different sites in many complex processes. The overall potential for dermal or inhalation exposure can therefore, although it may be low at particular sites or processes, not a priori be neglected. Therefore, taking account of the comments received during consultation, we still consider the original assessment of wide dispersiveness of uses appropriate. See also the (updated) background document (in particular parts "Releases from uses" in section 2.2.2.2 and "Prioritisation" in section 3.1) **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in this section. This response also considers the Chemical Agents Directive (and the medicinal products legislation.) In relation to Council Directive 92/85/EEC (Pregnant Workers Directive): the objective of this Directive is to protect the health and safety of women in the workplace when pregnant or after they have recently given birth and women who are breastfeeding; thus, this aims to encourage improvements in health and safety at the workplace, and in this case, for a defined sensitive group, through the assessment of risks at the workplace. In case the results of this assessment reveal the existence of a risk to the safety or health of the female worker, provision must be made for the worker to be protected. In addition, pregnant workers and workers who are breastfeeding must not be engaged in activities which have been assessed as revealing a risk of

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				exposure, jeopardizing safety and health, to certain particularly dangerous agents or working conditions. Whilst the Directive identifies substances with R-phrases relevant for reprotoxic potential for particular attention in an assessment, the Directive leaves the determination of the measures to be imposed to the employer. On this basis Directive 92/85/EEC does not seem to impose binding minimum requirements for controlling risks to human health in accordance with Article 58(2) of the REACH Regulation, as previously highlighted. Therefore, this Directive seems not to be a sufficient basis for exempting uses of N,N-Dimethylacetamide from authorisation.
21	2012/09/18 11:37	SPECTARIS e.V. Industry or trade association Germany	SPECTARIS comments on the ECHA´s draft of the 4th recommendation "Spectaris. Deutscher Industrieverband für optische, medizinische und mechatronische Technologien e.V." is a German industrial association for optical, medical and mechatronical technologies representing the medium-sized high tech industry in Germany. Within this function we send our comment to the draft of ECHA's 4th recommendation of N,N-Dimethylacetamid (DMAC) to be included in the Authorisation List. The use of DMAC as solvent for production of polysulfone membranes is described in literature as state-of-the-art. DMAC is known to be reprotoxic with a defined occupational exposure limit. As part of the Life Sciences Industry, the medical technology companies in Germany resp. Europe gener-ally have to fulfill high standards. Certification according to EN ISO 13485 corresponds to a highly controlled quality and safety during production process and for the finished medical device. Additionally, the companies have to fulfill regulations regarding employment protections defined by national laws (based on EU regulations) as well as regulations regarding protection of users and patients based on the MDD. According to Regulation (EC) No 1907/2006 (Reach), article 58, 2. and	Thank you for your comment and the information provided. As regards your exemption request, please see response to comment #33 in this section. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in this section. This response also considers the Chemical Agents Directive (and the medicinal products legislation.) The Medical Devices Directive (MDD, Directive 93/42/EEC) is intended to harmonise the laws relating to medical devices within the EU. In relation to legislation relating to medical devices, ECHA refers to recital 18 of Commission Regulation (EU) No 143/2011 of 17 February 2011, amending Annex XIV to REACH for the first time:

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			article 60, 2. the inclusion of DMAC in annex XIV of regulation (EC) No 1907/2006 (Reach) will lead to a double regulation for manufacturers of dialyzers containing polysulfone membranes, because: The♣ handling of DMAC during production is regulated e. g. in Germany by the 'Arbeitsschutzge-setz' (German Occupational Safety and Health Act) based on European regulations. The CE-approval of medical devices, which is♣ mandatory for marketing of the products within the EU is regulated by the Medical Device Directive (MDD 93/42/EEC). Inclusion of DMAC in annex XIV of regulation (EC) No 1907/2006 (Reach) will lead to a disad-vantage on the European market for medical technology companies with manufacturing site in Europe. These companies already fulfill the high European regulations for employment and environmental protection and for medical devices. Additional regulations arising from inclusion of DMAC in annex XIV (Reach) without any exceptions for medical devices producing companies would lead to disadvantages compared to dialyzer manufacturers from non-EU-countries.	In accordance with Article 60(2) of Regulation (EC) No 1907/2006, the Commission should not consider, when granting authorisations, the human health risks associated with the use of substances in medical devices regulated by Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices, Council Directive 93/42/EEC of 14 June 1993 concerning medical devices, or Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices. In addition, Article 62(6) of Regulation (EC) No 1907/2006 provides that applications for authorisation should not include the risks to human health arising from the use of a substance in a medical device regulated under those Directives. It follows that an application for an authorisation should not be required for a substance used in medical devices regulated under Directives 90/385/EEC, 93/42/EEC, or 98/79/EC if such a substance has been identified in Annex XIV to Regulation (EC) No 1907/2006 for human health concerns only. Therefore, an assessment as to whether the conditions for an exemption pursuant to Article 58(2) of Regulation (EC) No 1907/2006 apply is not necessary. Based on the above, ECHA would suggest that you examine whether the mentioned uses of your substance can be regarded as uses in medical devices in accordance with the MDD.
19	2012/09/17 22:31 See attachment *19_Section IV Attachment.doc*	Company Ireland	The potential inclusion of N,N-Dimethylacetamide 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 related to N,N-Dimethylacetamide presented in this annotation, should be considered in connection with the input provided by the European Federation of the Pharmaceutical industry (EFPIA). As noted previously in substance specific background documents developed by ECHA, N,N-Dimethylacetamide is one of a class of extremely useful solvents designated as polar aprotics to conduct reactions for	Please see response to comment #41 in this section. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in this section. This response also

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			producing intermediates and active pharmaceutical ingredients. In future, it is possible that there will be no alternative but to use N,N-Dimethylacetamide in the development stage of potential new products, intended to meet urgent medical needs. Should this occur after the latest application date, development efforts and active substance pharmaceutical manufacturing processes could be re-located outside the EU. It is our opinion, that the use of N,N-Dimethylacetamide as a solvent in the production of medicinal products 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.	considers the Chemical Agents Directive and the medicinal products legislation. Directive 2010/75/EU on industrial emissions (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 N,N-Dimethylacetamide which are assigned or need to carry the hazard statement H360D (i.e. toxic for reproduction 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 N,N-Dimethylacetamide which are assigned or need to carry the hazard statement H360D, '(…) 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'. The emission limits stated in the IED Directive are by reference to activities using greater than certain

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				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 in the other responses to comments referred to above.
18	2012/09/17 18:26	Pharmachemical Ireland Industry or trade association Ireland	Within the Pharmaceutical Industry, DMAC is used both in lab R&D and in the supply chain of Active Pharmaceutical Ingredients (API's). For the production of pharmaceuticals, DMAC is one of a class of extremely useful solvents designated as polar aprotics to support reactions for producing intermediates and API's. Rates and selectivity of certain reactions (e.g. nucleophilic substitutions) are substantially enhanced due to the solvent polarity and other properties. Polar aprotic solvents such as DMAC are essential for these reactions, since they prevent unreacted materials from being carried forward in the process stream, they minimise the formation of side products, and produce intermediates and API's of the highest quality.	Thank you for this information
17	2012/09/17 17:14	B. Braun Avitum AG Company Germany	1. Background: N,N-Dimethylacetamid (DMAC) was included in the Candidate List of Substances of Very High Concern (SVHC) by the European Chemicals Agency (ECHA) on December 19, 2011 (ECHA's decision ED/77/2011), according to article 57 (c), because DMAC is classified as toxic for reproduction 1B, H360D ('May damage the unborn child'). On June 20, 2012, ECHA has launched a public consultation on its draft recommendation of ten new priority substances (DMAC amongst others), to be included in the Authorisation List. The deadline for interested parties to submit comments is September 19, 2012. We, B. Braun Avitum AG, hereby take the opportunity to comment the 'Draft background document for DMAC' (ECHA, June 20, 2012). 2. Production Process: N,N-dimethylacetamide (DMAC) is an organic compound with the formula	Thank you for your comment the provided information. As regards information on the risks associated with your use, potential alternatives, and socioeconomic considerations, please see response to comment # 41 in this section. In relation to the assessment of the wide-dispersiveness (# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in this section. On alternative to authorisation risk management options, please see response to comment #8 in this section.

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			CH3C(O)N(CH3)2. Due to the high boiling point DMAC is widely used as a polar solvent in organic synthesis, for fibers (e.g. polyacrylonitrile) or hollow fiber membrane spinning solutions (e.g. polysulfone), and in the adhesive industry. It is also used in production of pharmaceuticals and plasticizers as reaction medium. The following facts are well known for DMAC: It is classified as toxic for reproduction and has a defined threshold value. DMAC is harmful by inhalation and skin contact and causes irritations to the eyes. The B. Braun Avitum AG has been selling dialyzers and filters for medical applications since 2004. The company is certified according to EN ISO 13485 as well as EN ISO 9001. Additionally B. Braun Avitum AG fulfills international regulations e.g. GMP as B. Braun sells products all over the world, e. g. USA, Canada, China. The dialyzer membrane is made of polysulfone, manufactured by a continuous wet spinning process, as it is state-of-the-art for hollow fiber production. DMAC is used as solvent in the spinning solution consisting of polysulfone (PSU) and poly-N-vinylpyrrolidone (PVP). The production of hollow fiber membranes is performed in a closed system, just as the recovery of the solvent (water/DMAC). Twice a year, the production process is interrupted due to maintenance works. According to known scientific literature, there is only one solvent, NMP (1-methyl-2-pyrrolidone), which could be possibly used instead of DMAC, but because of its similar chemical structure it has similar toxic properties. NMP is also included in the Candidate list of the ECHA, because of it's classification as reprotoxic. Within the B. Braun Avitum AG production process, a replacement of DMAC by another solvent would lead to an extremely high cost- and time-consuming process, influencing all registration certificates for all products. The handling and use of DMAC are regulated by the German Occupational Safety and Health Act (Arbeitsschutzgesetz) and related regulations, based on EU regulations for employment protection. We comply with the legal requirements in the production processes mentioned above (workplace exposure limits: 36 mg/m³) [TRGS 900 „Arbeitsplatzgrenzwerte"]. In spite of compliance with the threshold, pregnant employees are not allowed to work within the production area. As an additional safety measure for the employees, during restart of spinning process after maintenance work or limited breakdowns during production process, it is mandatory to wear a full body protection including	Please also note that REACH is an EU Regulation aiming to ensure a high level of protection of human health and the environment while enhancing competitiveness and innovation. The obligation to apply for authorisation is to ensure that risks are adequately controlled or that socio-economic benefits are outweighing the risks, while concomitantly it is a strong incentive to search for and develop suitable alternatives. As DMAC is toxic for reproduction, 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 DMAC will accordingly ensure that the health of workers in the EU involved in the uses of DMAC is protected. Authorisation does not ban or restrict the use of the substance as long as it is shown in the authorisation applications (and supported in the authorisation granting process) that either the risks arising from the use(s) applied for are adequately controlled or that there are no alternatives available and the socio-economic benefits are outweighing the risks arising from the uses. Information and concerns brought forward in your comments can be included in the application, should you decide to apply for authorisation of your uses of the substance or if your supplier applies for you. 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. See also response to comment #8 in this section.

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			breath mask. Even in case of exceeding the threshold of DMAC, inhalation, skin contact or eye irritation will be inhibited. To avoid any adverse effects for the environment, technological unavoidable gas emissions (exhaust) pass a high efficiency scrubber before emission (outside building). Transportation, storage and handling of the raw material DMAC is also controlled regarding national regulations. 3. Economic aspects: Dialysis is a very important blood purification procedure. In case of renal failure it is a life-replacement method. Dialysis is on the one hand the most important alternative to kidney transplant and on the other hand the most important renal replacement therapy in case of chronic renal failure and the only option for acute renal failure treatments. It is assumed that the number of patients suffering from chronic renal failure worldwide will double from currently about 2 million to the year 2020. Approx. 20% of dialysis patients worldwide live in Europe and need today around 50-60 million dialyzers annually. The number of people with kidney disease which potentially could lead to a chronic renal failure is much higher: about 5 million in Europe. More then 50 % of the dialyzers produced and sold in Europe are based on polysulfone membranes using DMAC as solvent [approx. 35 million dialyzers, B. Braun Avitum AG: about 5 million]. Inclusion of DMAC in annex XIV of regulation (EC) No 1907/2006 means a competitive disadvantage only for European manufacturers of dialyzers [e.g. high costs for registration, declaration of the used solvent on the finished medical device]. 4. Regulative aspects: Regulation (EC) No 1907/2006 (Reach), article 58, 2. states: 'Uses or categories of uses may be exempted from the authorization 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. […]' Regulation (EC) No 1907/2006 (Reach), article 60, 2. states: '[…] The Commission shall not consider the risks to human health arising from the use of a substance in a medical device regulated by […], Council Directive 93/42/ EEC of 14 June 1993 concerning medical devices […].'	**Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in this section. This response also considers the Chemical Agents Directive (and the medicinal products legislation.) In relation to the Medical Devices Directive, please see response to comment #21 in this section.

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			The specific use of DMAC as solvent for dialyzer production is already covered by the above referred articles of regulation (EC) No 1907/2006 (Reach), for the following reasons: • The use of DMAC within the production process is controlled by the German Occupational Safety and Health Act and related regulations. The use of DMAC under specific conditions, meeting the defined threshold value, does not lead to any risk for humans. This is controlled by German authorities. • The resulting product, which is a non-active medical device is controlled by the European Medical Device Directive (MDD 93/42/EEC) dated June 14, 1993 and latest amendments according to Directive 2007/47/EC dated September 5, 2007. B. Braun Avitum AG confirms with the CE-labeling and with the declaration of conformity of our non-active medical devices that the respective products are in compliance with the "essential requirements" of the MDD. That includes according to Article 3 and Annex I of MDD, that non-active medical devices of B. Braun Avitum AG are designed and manufactured in a way that, when used under the conditions and for the purpose intended, they will not compromise the clinical condition or the safety of patients nor the safety and health for users or third parties. This assessment was carried out as part of the B. Braun Avitum AG Risk Management System implemented according to EN ISO 14971, 'Medical devices - Application of risk management to medical devices'. Evaluation of biocompatibility of the non-active medical device was performed according to harmonized standard EN ISO 10993, 'Biological evaluation of medical devices'. 5. Summary: According to the above mentioned aspects: • missing hazard-free alternative for DMAC as solvent in the spinning process of polysulfone membranes • resulting double regulation through REACH because of: -> production environment regulated by national laws -> finished medical device regulated by MDD • disadvantage for European manufactures of polysulfone-containing dialyzers we, B. Braun Avitum AG, would like to initiate a discussion regarding an exceptional rule for our specific use of DMAC within the production process of non-active medical devices (dialyzers).	

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
16	2012/09/17 14:48	DuPont (U.K.) Industrial Limited Company United Kingdom	The information provided in this document is based on knowledge of DuPont and experience from manufacturing N,N-dimethylacetamide (DMAc) in the US and using DMAc for over 50 years. In Europe, DuPont produces a meta-aramid fibre in Asturias, Spain. We also provide information to clarify that there is no wide-dispersive use of DMAc in films and commented on the use in wire enamels. Our comments complement those submitted separately by CIRFS, the European Man-Made Fibres Association. CIRFS presents, on behalf of six man-made fibre producers, the overall arguments against the draft proposal for inclusion of DMAc on Annex XIV REACH. The information from the Man-Made Fibre industry clearly shows that DMAc should not be prioritized for inclusion on Annex XIV, and other risk management options (RMOs) such as Restriction would be more appropriate. Based on knowledge of DuPont about DMAc and the comprehensive data/explanations/ conclusions submitted in the confidential documents, the main points are: DMAc is used at a limited number of industrial sites in the EU, including only 6 man-made fibre production sites. The draft recommendation has incorrectly included DMAc as an impurity in articles as a use; this results in a significantly increased number of sites "using DMAc". Consequently, DMAc is currently ranked, inaccurately in our view, as having wide-dispersive use and uncontrolled releases. Worker, public and environmental exposure to DMAc from industrial operations, including meta-aramid fibre production, is demonstrated to be both well controlled and safe. There is no uncontrolled release or risk of harm to workers. Extensive data on the process and measured exposures are documented and explained. Worker, end-user and environmental exposure to residual DMAc in man-made fibres, including meta-aramid fibre and their products is negligible and well within safe limits. Potential releases from the fibre in processes along the value chain and in final applications are understood and clearly indicate that there is no risk from the residual content.	Thank you for your comment the provided information. As regards information on the risks associated with your use, potential alternatives, and socioeconomic considerations, please see response to comment # 41 in this section. In relation to the assessment of the wide-dispersiveness (# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in this section. On alternative to authorisation risk management options, please see response to comment #8 in this section.

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			Including DMAc on Annex XIV is not an effective risk management option. DMAc should not be prioritized when other solvents with a similar toxicity profile (such as NMP, DMF, NEP) are treated differently or are at different stages of the Authorisation process, resulting in the unintended consequence of preferring one SVHC over another SVHC due to different regulatory compliance requirements. Including DMAc on Annex XIV will substantially distort the Man-Made Fibre industry and threaten associated innovation in the EU. There is currently no commercially available alternative to DMAc as a solvent in the production of a meta-aramid with the equivalent functional properties. And that can be used in a wide array of applications in key European industries, and which would provide the socio-economic benefits of meta-aramid products. While alternative solvents have been investigated over many years, none have met stringent performance and human health criteria that would make them viable substitutes for the manufacture of a product with the particular and desirable safety and technical specifications of meta-aramid products. DuPont supports an EU wide Restriction of consumer and professional uses of DMAc. A targeted Restriction of the uses of DMAc is a more effective and coherent RMO than Authorisation to address concerns associated with professional and consumer exposures to DMAc.	
15	2012/09/17 14:33	MSCA United Kingdom	This substance has a high priority score, but there would appear to be a lack of suitable alternatives. Confirmation that there is no consumer use would be useful as it seems clothing and baby nappies do contain DMAC. Such uses may be better addressed through a targeted restriction. Authorisation is probably only of limited benefit as import of articles (e.g. films) that contain more than 0.1% would not be prevented and exposure would remain a possibility.	Thank you for your comment. The prioritisation for inclusion in Annex XIV is 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). Information on topics such as the availability and suitability of alternatives is not a criterion for prioritisation as, apart from proper control of risks arising from the uses of substances of very high concern, a further objective of authorisation is the progressive replacement of SVHCs by suitable alternative substances or technologies where these are economically and technically viable.

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				Indeed, Article 55 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 is no viable reason for adjourning the subjection of the 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. As regards the probable limited benefit of authorisation in relation to import of articles containing the substance, please note that REACH Article 69(2) requires ECHA to consider for all substances included in Annex XIV (after their sunset dates as defined in Annex XIV) whether the use of these substances in articles poses a risk to human health or the environment that is not adequately controlled. If it is considered that the risk is not adequately controlled ECHA shall prepare a restriction dossier in accordance with Annex XV.
14	2012/09/17 14:15	Company Denmark	Novo Nordisk acknowledges that authorisation under REACH is a relevant regulatory action to achieve and document safe use of substances of very high concern (SVHC). The use of N,N-dimethylacetamide (DMAC) by Novo Nordisk benefits from the unique dipolar aprotic solvent properties of DMAC which facilitate the extraction of Active Pharmaceutical Ingredients	Please see response to comment #30 in this section.

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			(API) with high quality and a minimum content of impurities. We are aware that EFPIA has submitted a comment in the public consultation in which an exemption from authorization is requested for the use of DMAC in the production of medicinal products. Irrespective the decision whether or not DMAC will be included in Annex XIV of REACH, Novo Nordisk wants to point out that our use of DMAC in the production of insulin is already adequately controlled. The handling of DMAC in its bulk form as well as during the mixing, reaction and extraction processes takes place under highly controlled procedures and by use of closed systems. Novo Nordisk has initiated a thorough assessment of the potential occupational and environmental exposure to DMAC resulting from the production of insulin. The exposure assessment will lead to documentation in quantitative terms confirming that Novo Nordisk's use of DMAC is adequately controlled. In line with the evaluation in the Annex XV dossier, it is the opinion of Novo Nordisk that there are currently no possibilities to replace DMAC with substances with less hazardous properties. It is very difficult to substitute substances used for the production of APIs as the processes have been carefully refined and optimised, and even minor changes in the production processes may compromise the quality of the API. Novo Nordisk is continuously optimising the production with the aim to further reduce emissions of DMAC and, if possible, identify alternative processes and chemistry. Time is needed to identify possible alternatives and confirm their technical and economic feasibility.	
13	2012/09/14 16:29 See attachment *13_DMAC_Annex XIV Recommendation .pdf*	Industry or trade association Belgium	Please find our comments in our attached pdf document (in section IV).	Thank you for your comment. **Exemption request** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in this section. This response also considers the Chemical Agents Directive (and the medicinal products legislation.) In relation to the Pregnant Workers Directive, please see the response to comment #21A in this section.

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
				Proportionality of authorisation requirement As regards the proportionality of inclusion of DMAC to Annex XIV, please note that REACH is an EU Regulation aiming to ensure a high level of protection of human health and the environment while enhancing competitiveness and innovation. The obligation to apply for authorisation is to ensure that risks are adequately controlled or that socio-economic benefits are outweighing the risks, while concomitantly it is a strong incentive to search for and develop suitable alternatives. The workability of the authorisation process justifies the need for a gradual inclusion of substances in Annex XIV. To prioritise substances to Annex XIV the criteria set out in Article 58(3) are used following the agreed approach. As DMAC is toxic for reproduction, there is a strong societal interest to protect humans from risks potentially arising from its uses. An authorisation requirement for DMAC will contribute to ensure that the health of workers in the EU involved in the uses of this substance is protected while it has not yet been replaced by suitable alternatives. Authorisation does not ban the use of the substance as long as it is shown in the authorisation applications (and supported in the authorisation granting process) that either the risks arising from the use(s) applied for are adequately controlled or that there are no alternatives available and the socio-economic benefits are outweighing the risks arising from the uses. Pursuant to Art. 60 REACH authorisation shall be granted if the risks to human health and environment posed by a use are adequately controlled. If the risk is not considered to be adequately controlled, an authorisation may be granted if socio-economic benefits outweigh the risk to human health and the environment and if there

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				are no suitable alternative substances or technologies. Information and concerns brought forward in your comments, e.g. on the availability and suitability of alternatives and the need to get their use certified or approved, 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. If included in an application for authorisation, this information may impact the decision on granting an 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. Finally, we note that import of articles containing DMAC is indeed not directly affected by the authorisation requirement and a restriction process has to be applied if there is a need to restrict such import. After the sunset date defined in Annex XIV for a given substance, ECHA has an obligation under Article 69(2) to consider whether the substance in articles poses a risk and, if yes, prepare an Annex XV restriction dossier.
12	2012/09/14 12:02	Company France	Inclusion of DMAC in Authorization list is not an adequate exposure control method for the enamel production and wire enamelling/coating industry	Please see responses to comment #8 in this section, as well as to the same comment (#12) in section III of this document.
11	2012/09/13 11:58	Company Ireland	Within the Pharmaceutical Industry, DMAC is used both in lab R&D and in the supply chain of Active Pharmaceutical Ingredients (API's). For the production of pharmaceuticals, DMAC is one of a class of extremely useful solvents designated as polar aprotics to support reactions for producing intermediates and API's. Rates and selectivity of certain reactions (e.g. nucleophilic substitutions) are substantially enhanced due to the solvent polarity and other properties. Polar aprotic solvents such as DMAC are essential for these reactions, since they prevent unreacted materials from being carried forward in the process stream, they minimise the formation of side products, and produce intermediates and API's of the highest quality. In some cases, the properties of DMAC are unique in effecting a desired reaction reactivity, selectivity, solubility, or purification and no	See response to comment #22 in this section. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in this section. This response also considers the Chemical Agents Directive and the medicinal products legislation.

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			comparable performance with any other solvent is known or the alternative solvents pose a greater environmental, occupational health, or other concern. There are other polar aprotic solvents with similar physical or chemical properties (albeit of lower polarity) that could potentially be used in place of DMAC in some API manufacturing syntheses. The most common 'direct' alternative may be DMF (N,N-dimethylformamide). Others include formamide, N-methylformamide, N-methyl pyrrolidon and N-methylacetamide. However, these alternatives carry essentially the same health hazard as DMAC. Some of these solvents are already on the REACh Candidate List. In addition, these solvents have lower polarity and for some purposes different reactivity; the replacement of DMAC with such solvents could lead to incomplete reactions and side products that impact the safety and quality of the API. Moreover, this would result in an increase in waste streams. The manufacture of APIs and associated intermediates are performed in enclosed reactor trains in accordance with Good Manufacturing Practices (GMP). DMAC (and other solvents) are introduced into the reactors via transfer systems designed to minimize environmental release, by trained personnel using appropriate engineering controls and/or protective equipment, and are thus contained within the process stream. Occupational exposure is also controlled through compliance with the Chemical Agents Directive (98/24/EC). Since the residual amount of DMAC in the eventual product (drug substance) is safety-limited by the ICH Q3C (Guideline for Residual Solvents), in practice virtually all the DMAC used during manufacture would be present in the waste streams that are disposed in accordance with local environmental regulations. Thus, the risks of environmental exposure of DMAC in the pharmaceutical manufacturing environment are minimized by the equipment design and operational controls; disposal and record-keeping procedures exist within the governance of the quality system.	
10	2012/09/13 11:51	Company Belgium	Within the Pharmaceutical Industry, DMAC is used both in lab R&D and in the supply chain of Active Pharmaceutical Ingredients (API's). For the production of pharmaceuticals, DMAC is one of a class of extremely useful solvents designated as polar aprotics to support reactions for producing intermediates and API's. Rates and selectivity of certain reactions (e.g.	See response to comment #22 in this section. **Art 58(2) exemption response**

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			nucleophilic substitutions) are substantially enhanced due to the solvent polarity and other properties. Polar aprotic solvents such as DMAC are essential for these reactions, since they prevent unreacted materials from being carried forward in the process stream, they minimise the formation of side products, and produce intermediates and API's of the highest quality. In some cases, the properties of DMAC are unique in effecting a desired reaction reactivity, selectivity, solubility, or purification and no comparable performance with any other solvent is known or the alternative solvents pose a greater environmental, occupational health, or other concern. There are other polar aprotic solvents with similar physical or chemical properties (albeit of lower polarity) that could potentially be used in place of DMAC in some API manufacturing syntheses. The most common 'direct' alternative may be DMF (N,N-dimethylformamide). Others include formamide, N-methylformamide, N-methylpyrrolidon and N-methylacetamide. However, these alternatives carry essentially the same health hazard as DMAC. Some of these solvents are already on the REACh Candidate List. In addition, these solvents have lower polarity and for some purposes different reactivity; the replacement of DMAC with such solvents could lead to incomplete reactions and side products that impact the safety and quality of the API. Moreover, this would result in an increase in waste streams. The manufacture of APIs and associated intermediates are performed in enclosed reactor trains in accordance with Good Manufacturing Practices (GMP). DMAC (and other solvents) are introduced into the reactors via transfer systems designed to minimize environmental release, by trained personnel using appropriate engineering controls and/or protective equipment, and are thus contained within the process stream. Occupational exposure is also controlled through compliance with the Chemical Agents Directive (98/24/EC). Since the residual amount of DMAC in the eventual product (drug substance) is safety-limited by the ICH Q3C (Guideline for Residual Solvents), in practice virtually all the DMAC used during manufacture would be present in the waste streams that are disposed in accordance with local environmental regulations. Thus, the risks of environmental exposure of DMAC in the pharmaceutical manufacturing environment are minimized by the equipment design and operational controls; disposal and record-keeping procedures exist within	In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in this section. This response also considers the Chemical Agents Directive and the medicinal products legislation.

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			the governance of the quality system.	
9	2012/09/12 17:38	Industry or trade association United States	The National Electrical Manufacturers Association (NEMA), representing manufacturers of electrical and medical imaging equipment, appreciates the opportunity to comment on behalf of its Magnet Wire Section on the current public consultation for the European Chemicals Agency's (ECHA) draft recommendation of priority substances to be included in the REACH Authorization List, specifically, N,N-dimethylacetamide (DMAC). Magnet wire (also known as winding wire) is absolutely integral to the efficient production, conversion, and management of electrical energy. It is beyond dispute that the world has entered a period of ever-growing demands on production and management of electricity. The International Atomic Energy Agency (IAEA) has indicated that global electricity demand is expected to double between 2000 and 2030 (see http://www.iaea.org/Publications/Magazines/Bulletin/Bull461/power_to_the_people.html). In turn, there is an associated demand for high-performance magnet wire. Some of the most advanced magnet wire products, such as those used on wind turbines, rely on DMAC and/or 1-methyl-2-pyrrolidone (NMP). (DMAC is often used as a substitute for NMP.) Other magnet wire enamel chemistries do not provide the high performance available from enamels based on NMP and DMAC solvent chemistry. NMP and DMAC are in a unique class of solvents referred to as aprotic solvents. These solvents are required for producing high-performance enamels, such as polyamide imides and polyimides; we are aware of no viable alternatives. It is therefore imperative that DMAC and NMP remain available for production of high-end enamels, to in turn manufacture the high-performance magnet wire that the world increasingly demands. Reducing availability of DMAC and/or NMP could perhaps preclude the production of a necessary commodity like high-performance magnet wire. This would be entirely contrary to the ongoing worldwide drive for more intelligent management of energy.	Thank you for your comment. As regards the information on socioeconomic considerations, please see response to comment # 41 in this section. Please also note that use of DMAC will still be possible in the future, i.e. after the sunset date, provided a use-specific and applicant-specific authorisation is applied for and granted.
8	2012/09/12 17:29	Company United Kingdom	For the production of pharmaceuticals, DMAC is one of a class of extremely useful solvents designated as polar aprotics to support reactions for producing intermediates and Active Pharmaceutical Ingredients (API's). Rates and selectivity of certain reactions (e.g. nucleophilic substitutions)	Thank you for providing your opinion. Please note that in the process of assessing whether a substance on the Candidate List has priority for inclusion

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			are substantially enhanced due to the solvent polarity and other properties. Polar aprotic solvents such as DMAC are essential for these reactions, since they prevent unreacted materials from being carried forward in the process stream and minimise the formation of side products. There are other polar aprotic solvents with similar physical or chemical properties that could potentially be used in place of DMAC in some API manufacturing syntheses. The most common 'direct' alternative may be DMF (N,N-dimethylformamide). Others include formamide, N-methylformamide, N-methyl pyrrolidon and N-methylacetamide. However, these alternatives carry essentially the same health hazard as DMAC. Some of these solvents are already on the REACh Candidate List and some can be expected to be included in the near future. With this similar solvents at different stages of the candidate list, authorisation list or even possibly future restriction processes, it will be very difficult for the Pharma industry to fully assess the impact of authorisation, develop a strategy and plan for potential substitutes. We ask that ECHA considers this when selecting these solvents for potential authorisation and/or restriction candidates.	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 or its particular uses. Note also that authorisation is not comparable to a ban or restriction of a substance but it is rather to a requirement to request authorisation for carrying out particular uses with the substance. Substances included in Annex XIV maybe granted an authorisation if the applicant can show adequate control of risks arising from the applied for uses or if there is no suitable alternative available to the substance and the socio economic benefits of the use outweigh the associated risks for health and environment. The meaning of "(suitable) alternative" in the context of authorisation means the possibility of replacement of the substance in a particular use by another in technical and economic terms feasible substance or technology, thereby reducing the overall risk arising from the use in question. In cases where you consider substitution, we would suggest to comparatively assess the feasibility aspects and the overall risks to human health and the environment exerted by the substance / technology you currently use and of any potential alternative substance or technology.
7	2012/09/12 15:20	MSCA Norway	The Norwegian CA supports the prioritization of N,N-Dimethylacetamide (DMAC) for inclusion in Annex XIV.	Thank you for your opinion.
4	2012/09/11 10:51	Company Germany	Introduction The recommended inclusion of DMAC in Annex XIV poses a critical burden for certain European medical device manufacturers and endangers lifesaving treatments, especially for end stage renal disease (ESRD)	Thank you for your comment and the information provided. As regards information on the risks associated with your

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			patients in the European Union and worldwide. For medical devices the inclusion of DMAC would be a double regulation and is not necessary at all. The existing Community legislation on occupational safety and on medical devices already regulates safety and risk control during manufacturing and use of the concerned medical devices and the materials used in manufacturing. Further regulation would not result in an improvement in safety and risk control. Comments on priorisation The ECHAs recommendation to include DMAC in Annex XIV is based on the assumption that very high volumes of DMAC are widely used in a dispersive manner by industry sectors and in products (e.g. textile fibres), which are subject to a relative low level of regulation. This is not the case at all for DMAC used in medical device production. In the medical device industry DMAC is an essential process solvent for production of membranes, used for example in dialysis treatment and other lifesaving extracorporeal therapies. DMAC is used as solvent within the highly specialized, controlled and regulated membrane manufacturing process. This use is limited to few sites (<10 within EU) and represents, regarding the needed quantities, only a minor use of DMAC (estimated total consumption < 1%). The regulation of the finished product as medical device by the applicable Community legislation, e.g. 93/42/EEC, already ensures a high level of protection of health and safety. This risk control already ensures that hazardous substances and their risks are appropriately reduced or eliminated. Relevance of DMAC in health care The lives of approximately 2 million ESRD (end stage renal disease) patients worldwide, approximately 300,000 of whom are within the European Union, depend on the performance and reliability of the applied treatment and the medical devices used. Furthermore, DMAC based membranes are required for medical devices used in other critical care and ambulatory extracorporeal treatments. Affected indications include liver failure as well as serious rare and orphan diseases.	use, potential alternatives, and socioeconomic considerations, please see response to comment # 41 in this section. As regards the possibility for alternative to authorisation risk management options, please see response to comment #8 in this section. In relation to the assessment of the wide-dispersiveness (# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in this section. As regards the proportionality of authorisation, please see response to comment #13 in this section. The inclusion in Annex XIV is per substance and not per use (or installation). Therefore screening of release potential in the prioritisation phase does not assess the exposure levels from single uses (at specific sites), but aims to deduce whether there are uses/situations where exposure may potentially not be controlled (mainly for workers and consumers in the case of CMR). The use and user specific conditions can be reflected in the authorisation application and they will be taken into account by ECHA's Committees when developing their opinions on the applications and by the Commission when taking the final decisions. In a potential application for authorisation, the exposure assessment shall consider the emission during all relevant parts of the life-cycle of the substance resulting from each of the uses applied for. The life-cycle stages resulting from identified uses cover, where relevant, the service life of articles. In this context, a very low residual concentration of DMAC after a certain stage of production can be given as justification for not considering, in the exposure assessment, the subsequent

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			The properties of the membranes in the needed filters and dialyzers must satisfy the highest standards regarding safety, biocompatibility and medical performance. All of these aspects are significantly influenced by the membrane material and structure. Only few polymers on an industrial scale meet the requirements for state of the art membranes for the concerned medical devices. Highly specialized solvent based manufacturing processes transform these polymers into the membranes with defined properties crucial for required medical performance and safety. Solubility of the polymers and the solvent's influence on the membrane properties (e.g. pore structure, surface chemistry, permeability, selectivity) restrict the selection of solvents. A significant portion of the filters used for renal replacement therapy (e.g. dialyzers) and other extracorporeal therapies worldwide are produced with DMAC. The DMAC based membranes are state-of-the-art for safety, biocompatibility, treatment outcome and medical treatment costs worldwide. The applied manufacturing processes ensure, as required by the medical device legislation, that DMAC is not present in the finished devices. DMAC alternatives in manufacturing of medical devices Less hazardous solvents meeting the medical, technical and regulatory requirements for the concerned membranes are NOT available. None of the solvents listed in the draft ECHA background document (DMSO, sulfolane, acetone, acetonitrile) is suitable to replace DMAC in the affected production of medical device membranes. Besides the mentioned DMAC-based membrane production, significant alternative membranes for the described applications are currently only produced using NMP (1-methyl-2-pyrrolidone). NMP, which is also classified as reproductive toxic 1B and identified as SVHC Candidate. Economic relevance for European health care industry The authorization requirement will only restrict European production sites of medical devices. Due to the applicable existing Community legislation on medical devices	life-cycle steps. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in this section. In relation to the Medical Devices Directive, please see response to comment #21 in this section.

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			i.e. 93/42/EEC and REACH Article 60/2 medical device production outside the European Union and imports into the EU will neither be affected nor restricted by REACH regulations on the authorization of Substances of Very High Concern. The proposed inclusion of DMAC for medical devices in Annex XIV poses an improper discrimination of the concerned European medical device manufacturers related to the Community market and will also constrain the competitiveness of European exports. In addition, the different legislative approaches and timelines chosen for DMAC and NMP, the second important solvent, will lead to further market distortion in and outside EU.	
1	2012/07/20 12:47	Company United Kingdom	Use in the Pharmaceutical Industry: Although use of Active Pharmaceutical Ingredients (APIs) in secondary pharmaceutical production is not covered by the REACH regulations, the process for manufacture of these APIs is within the scope of REACH. N,N-Dimethylacetamide, or DMAC, is one of a class of extremely useful solvents designated as polar aprotics. The physical properties of these solvents make them an attractive choice from a chemistry perspective in the synthesis of (APIs) and associated intermediates. Advantages of DMAC include: • DMAC offers generally high solubility of many APIs and intermediates, which often have very poor solubility in less polar solvents. This facilitates processes that require minimal solvent quantities, compared with the much larger volumes of other solvents that may be required. • DMAC additionally offers sufficient solubility of many inorganic reagents (e.g. acids & bases) that facilitates chemical reactions that would not be practicable or robust in many other organic solvents. • Reaction rates of certain reactions (e.g. nucleophilic substitution) are substantially enhanced due to the solvent polarity. Polar aprotic solvents such as DMAC are essential for these reactions, since they prevent unreacted materials from being carried forward in the process stream, minimize the formation of side products, and produce intermediates and API of the highest quality.	Please see response to comment #30 in this section.

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			• The use of these solvents can be essential (due to their relatively low acidity) when strong bases are employed as these materials would be completely consumed by side reactions if protic solvents were used. • Water miscibility – for example facilitating precipitation, and subsequent isolation, of products from reaction liquors through the addition of water as an anti-solvent. • A high boiling point (166oC) – allowing reactions to be carried out at much higher temperatures than would be achievable in many organic solvents, without the need to operate under pressure (often not operationally feasible in typical pharmaceutical reactors, and inherently of greater operational hazard). An additional benefit is that the potential for solvent emissions associated with processing is less than those associated with many other solvents. DMAC is therefore used as a solvent within API research and development laboratories, development manufacturing pilot plants and commercial manufacturing plants. The manufacture of APIs and associated intermediates are performed in enclosed reactor trains in accordance with Current Good Manufacturing Practices. DMAC (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. Emissions to atmosphere are regulated by local environmental legislation. All medicines are tested for safety through extensive and demanding clinical trials and any issues related to solvent content would be well documented and controlled. Additionally the levels of residual solvents in API's are tightly controlled to low concentrations, that are internationally agreed and are based on toxicology data, and all API's undergo rigorous testing for solvent content before release to market. Therefore, in practice all the DMAC used during manufacture would be present in the waste streams that are then disposed of in accordance with local environmental regulations. Thus, the risk of environmental exposure of DMAC in the API manufacturing environment are controlled by the equipment design and operational controls; disposal, and record-keeping procedures under the oversight of the quality system. A key point of consideration for the pharmaceutical industry is the regulatory implications that may be associated with changing the solvent	

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			used in any stage of a commercial API manufacturing process that is registered with the appropriate regulatory health authorities. Changes to such processes invariably require extensive redevelopment of processes and associated interaction/authorisation from health authorities in order to ensure product quality, efficacy and patient safety is not compromised. Typically, changing a commercial process would necessarily involve a lead time of one to multiple years, large amounts of work and significant associated costs. In practice API customers would source the API from outside the European Union manufactured by the current route rather than undertake this re-registration of the process. In a worst case scenario this may lead to cessation of manufacture of certain pharmaceuticals within the European Union with a consequent detrimental effect on the health of the population. There are other polar aprotic solvents with similar physical properties that could potentially be used in place of DMAC in some API manufacturing syntheses. The most common 'direct' alternative is DMF (N,N-dimethylformamide). Others include formamide, N methylformamide and N-methylacetamide. However, these alternatives also carry essentially the same health hazard as DMAC. The replacement of DMAC with solvents having lower polarity could lead to incomplete reactions and side products that impact the safety and quality of the API. This might increase waste streams.	

II - Transitional arrangements. Comments on the proposed dates:

#	Date	Submitted by (name, Organisation/MSCA)	Comment	Response
46	2012/09/19 22:02	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 – see comment #37 in this section.
45	2012/09/19 21:46	Company Portugal	The acrylic fibre (and the articles obtained with it) is a long and a very complex supply chain. Acrylic fibre production is at the beginning of this supply chain. Any changes at the beginning have consequences for all subsequent stages. The acrylic fibre producers have developed several fibre properties that have been improved step by step resulting in a better end-use product. These properties are conditioned by the dope preparation and the spinning process where DMAC is used and it has an important contribution. It is very unlikely that the developed properties can be achieved in time period of two years - Mainly for special fibres (precursors and technical fibres). See item IV (Review periods for specific uses).	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

			Above considerations ask for a longer transitional arrangement than the proposed 2 years.	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.
41	2012/09/19 17:10	Federchimica Industry or trade association Italy	See above	See response to your comment #41 in section I of this document.
37	2012/09/19 11:07	MSCA Sweden	We agree with the proposed dates.	Thank you for your comment. 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, originally resulting in a combination of application/sunset dates for strontium dichromate of 21/39 months. 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 DMAC to 21 months after EiF.
36	2012/09/19 10:39	Company France	the proposed date are technically not realistic, because even if we find a substitute, it takes few years to modify the national drug product registrations for our pharmaceuticals customers	See response to comment #45 in this section.
25	2012/09/18 15:12	CIRFS: European Man-made Fibres Association Industry or trade association Belgium	The textile fibre supply chain is a very complex supply chain. Man-made Fibres (MMF) are at the beginning of this supply chain and changes at the beginning have consequences for all subsequent stages. MMF producers have been using DMAC for decades, and over that period several fibre properties have been improved step by step resulting in a better end-use product. It is very unlikely that the same properties will and can be achieved in a very limited time period. Some fibres go into high-tech and high-protective applications, where fibres can only be changed after very stringent, costly and long lasting (years) approval procedures. Above considerations ask for a longer transitional arrangement than the proposed 24 months.	See response to comment #45 in this section.
4	2012/09/11 10:51	Company Germany	time frame for medical devices The high level of safety and regulation required for development and production of medical devices inside the European Union requires time and cost intensive research, development and risk control, including clinical trials. Production processes and equipment is highly specialized and customized hence causing prolonged planning, implementation and installation time. Even if there was not a current lack of less hazardous alternatives for DMAC in the concerned medical device productions, the proposed sunset date would neither be sufficient to adequately eliminate DMAC in these processes nor to substitute for current European production capacities to ensure supply of the required number of medical devices.	Please note that the sunset date does not need to consider the timeframe in which it may be possible to substitute the substance in question in its uses. See also response to comment #45 in this section.

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

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
47	2012/09/19 22:21	ChemSec International NGO Sweden	Being such a hazardous substance, no use should be granted a generic exemption from authorisation.	Thank you for your opinion.
45	2012/09/19 21:46	Company Portugal	We are of the opinion that DMAC do not need authorization because: - DMAC has an i-OEL with skin notation. This has resulted in adequate control and protection (including skin protection) of the workers at industrial operations from chemical risks; - The acrylic fibre (and man made fibre) producers have implemented adequate control and monitoring measures, including regular reporting to authorities; - The acrylic fibre (and man made fibre) producers have implemented appropriated procedures to protect the workers at the different places where DMAC is used, they monitor the work place and the workers have training / education about DMAC risks and protection; - The acrylic fibre (and man made fibre) producers have occupational health services that monitors the health of workers; - DMAC is a residual impurity in the fibre, embedded in the fibre, which is mainly removed by the washing and dyeing processes. Potential risk related to airborne DMAC emissions from the fibre is below and appropriately manageable by air management at the converting operations; Taking the above arguments in consideration, DMAC does not need to be included in Annex XIV but they should lead to an exemption for the use of DMAC at acrylic fibre production (and man made fibre).	**Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in Section I. This response also considers the Chemical Agents Directive.
43	2012/09/19 18:40	Dralon GmbH Company Germany	N, N-Dimethylacetamid (im weiteren Text DMAc genannt) wird bei der Dralon GmbH seit Jahrzehnten als Lösungsmittel in der Polyacrylfaserherstellung eingesetzt. Die Verwendung von DMAc unterliegt seit ebenso langer Zeit, z. B. den Vorgaben aus dem Gefahrstoffrecht, dem Bundesimmissionsschutzgesetz und seinen Verordnungen, der TA Luft, dem Abfallrecht und dem Wasserhaushaltgesetz. Die durch den Gesetzgeber vorgegebenen Arbeitsplatzgrenzwerte (AGW,	Thank you for your comment and the provided information. As regards the information on risks associated to your use, alternatives and socioeconomic considerations, please see response to comment # 41 in section I. In relation to the assessment of the wide-dispersiveness

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
			TRGS 900) und Biologische Grenzwerte (BGW, TRGS 903) werden regelmäßig überwacht. Durch die vorhandenen Richtlinien und Gesetze auf nationaler und europäischer Ebene ist der Umgang mit DMAc lückenlos geregelt. Die bereits genannten Regelungen zum sicheren Umgang mit DMAc schützen die Umwelt und unsere Mitarbeiter umfassend. Ein Risiko für den nachgeschalteten Anwender und den Endverbraucher ist bei bestimmungsgemäßer Verwendung ausgeschlossen. Ein nicht ausreichend beherrschtes Risiko ist somit nicht vorhanden. Eine Ausnahme für die Verwendung von DMAc als Lösemittel in der Chemiefaserherstellung werden wir favorisieren. Die Verwendung von DMAc erfolgt von der Annahme über Lagerung bis zur Dopeherstellung in geschlossenen Systemen. Die Kontaktmöglichkeiten während dieser Anwendungen sind bei bestimmungsgemäßen Betrieb der Anlagen nur geringst. Die Expositionsszenarien entsprechen hier Anforderung der Stufe PROC 2. Die Anlagen in der Spinnerei entsprechen PROC 4. Hier wird die Dopelösung durch Spinndüsen gepresst und im Koagulationsbad ausgefällt. Die bei dem Institut für Arbeitssicherheit der Deutschen gesetzlichen Unfallversicherung erhobenen Daten zur Erstellung von REACh-Expositionsszenarien für N, N-Dimethylacetamid in der Textilindustrie bestätigen, dass auch beim nachgeschalteten Anwender keine Gefährdung der Mitarbeiter vorliegt. Wir können diese Aussage bestätigen, nachdem wir einzelne Tätigkeiten der Anwender nachempfunden und mit Messungen belegt haben. Eine Ausnahme für die Verwendung von DMAc als Lösemittel in der Chemiefaserherstellung werden wir favorisieren.	(# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in section I. In regard to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I.
41	2012/09/19 17:10	Federchimica Industry or trade association Italy	1) Pharmaceutical use DMAC is used as solvent in multistep synthesis of pharmaceutical intermediates before to get the final active pharmaceutical ingredients (API). Batch synthesis runs in multipurpose plants where workers' exposure is minimized by the presents of local exhaust ventilation (LEV). In addition are used loading system for the solvent (critical phase) specifically planned in order to reduce exposure. We further highlight that in the loading phase, drums are put inside aspired box where the fumes finish in a treatment system.	Thank you for your comment and the provided information. In relation to the assessment of the wide-dispersiveness (# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in section I. Please see also response to comment #4 in section I.

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			The staff involved in the procedure, included the staff in charge of maintenance operations, is properly trained and defended by appropriate protective equipment. The use of this substance as solvent in industrial plants for production of intermediates and API must already comply with the GMP rules and to the authorization of national and foreign pharmaceutical agencies. This type of use occurs under strictly control condition and for this reason we ask that must be excluded from the authorization procedure under Reach. 2) Industrial coatings On the basis of Article 58.2 of the REACH Regulation, we submit that the use of DMAC for "industrial coating" (with specific reference to the case of the enamels for electrical wire insulation in the automotive division) should be exempted from REACH authorization for the presence of existing EU legislation, and in particular Directive 98/24/EC (CAD) on the protection of workers, Directive 2008/1/EC (IPPC) and Directive 2010/75/EC (IED) concerning the "integrated pollution prevention and control" which are existing EU legislation that properly control the risks to environment and/or the human health for this use. Indeed, Directive 98/24/EC is a Directive based on Article 118a of the EC Treaty, which provided for the adoption of minimum requirements in order to guarantee a better level of protection for the safety and health of workers and which allowed Member States to apply stricter (but not less stringent) requirements under certain conditions Within EU framework, a Community-level occupational exposure limit (OEL) value was established on the basis of Directive 2000/39/EC. Implementing such a limit is effective in limiting the risk to workers: OEL (EU): 10 ppm (36 mg/m3) as an 8 hour Time Weighted Average (TWA); 20 ppm (72 mg/m3) as a 15 min STEL. Note: skin Additionally a Biological Exposure Index (BEI) has been derived by the American Conference of Governmental Industrial Hygienists (ACGIH). The BEI provides a measure of total systemic exposure and is based on measurement of the DMAC metabolite monomethylacetamide (MMAc) in urine in end of shift samples. The BEI is 30 mg of MMAc/g creatinine. Ultimately the presence of the above mentioned existing EU legislation and exposure limits makes the risks of DMAC for "industrial coatings" properly	**Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the Chemical Agents Directive. In relation to the Industrial Emissions Directive, please see response to comment #19 in Section I.

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			controlled.	
40	2012/09/19 16:24	Company Turkey	Point 2.2.2.2. "Man-made fibres (20-25%) REACH legislation 1907/2006, Art. 58 (2) AKSA,the biggest acrylic fiber producer of the world, situated in Turkey has declared, that we are willing to improve our wet spinning process by increasing the washing time in order to have a bigger cleaning effect of DMAC without reducing the speed of production and by doing so, the final fiber will have a DMAC-content much lower than 0,1 % which is already aproved by TESTEX with our eko-tex certificate as being below the 0.1%.. This fibers are also being imported into the EU. Comments to proposed alternatives Alternative DMSO Due to different reasons, we do consider DMSO not as a general substitute for DMAC: a) In the fiber production it is not suitable, as intrinsic properties will cause problems with the operational conditions (melting point), will cause concern due to decomposition products, that will form when the fiber is dried by heat evaporation (boiling point), which are hard to wash off and it causes garlic odour. Furthermore, there is no to only negligible consumer exposure via fibers. b) It is assumed, that DMSO is already used wherever possible due to the regulations being of advantage for DMSO. c) DMSO could be a substitute for paint strippers and solvent cleansers. Alternative DMI We see two reasons for not considering DMI as a suitable substitute for DMAC. The first is due to no experimental data being available while the structural similarity alerts the concern for reproduction toxicology, especially for the fertility and maybe even developmental effects. The second reason is the missing biodegradability of DMI. With 90 % of the DMAC release is via the fiber industry, this will raise a persistence issue. Alternative NEP This product is expected to be classified CMR 1 a/b at a not so far point in time and is therefore not suitable as a substitute.	Thank you for your comment and the provided information. In regard to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I.
39	2012/09/19 15:48 See attachment	Company Belgium	Chapter 2.2.2.2: Uses and releases from uses Main uses 1. General comments * Use descriptors	Thank you for your comment and the provided information.

#	Date	Submitted by (name, Organisation/ MSCA)	Comment	Response
	39_Comments DMAC.doc		We recommend to correct the uses that are described in the background document. DMAc is mostly used in closed industrial installations, and this for chemical synthesis. This would be a non-wide dispersive use. High volumes of DMAc are used, but the number of customers is limited and the product is mostly used in closed production system. DMAc for chemical industry is mostly as a solvent under controlled conditions, but it is not classified as an intermediate. DMAc is not transformed into another product. In a lot of cases, DMAc will also be recovered. So DMAc there will be only some residual amounts in the final product. The recovered DMAc is in general treated in a sewage treatment plant. Since DMAc is degraded very efficiently, the release to the environment will be minimal. * Authorization of DMAC use for chemical synthesis If we take the existing risk management measures into consideration, we think that authorisation for the industrial uses (meaning chemical synthesis) are disproportionate. In cases were DMAc is used in pharmaceutical or agrochemical applications, the compositions and the production process are part of the registration file. Changing the solvent would mean that the entire registration has to be revised. And often these registrations need to be repeated per country. The production and use of DMAc is adequately controlled, therefore bringing DMAc under authorisation would bring unnecessary costs and administrative work for the registrants. In addition, it will not be possible to foresee any forecasts for this product as there is the uncertainty of the authorisation. This would be a burden for EU producers, while this is not the case for non-EU producers. Since DMAc is only found at residual levels in final products, these can still be imported in the EU without any extra work. *Pharmaceutical use: DMAc is mainly used as a process solvent (synthesis of active ingredients) in the pharma industry. DMAc is a class II solvent and regulated as such by the pharmaceutical regulations. The residual amount is limited to 0.1%. Direct use in the pharmaceutical industry cannot be regulated by REACH, this is outside the scope of the regulation.. To eliminate these uses, a change in the pharma regulation would be required. *Agrochemical use DMAc is only used for the production of agrochemicals, or in the quality control service. Since DMAc is classified as a CMR cat 1B, the use in agrochemicals is already	As regards your proposal for restriction for the use associated with paint strippers, please see response to comment #34 in section I. In regards to the information on risks associated with specific uses, alternatives and socioeconomic considerations, please see response to comment # 41 in section I. In relation to the assessment of the wide-dispersiveness (# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in section I. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the Chemical Agents Directive (and the medicinal products legislation.) In relation to the Pregnant Workers Directive, please see response to comment #21A in section I.

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			prohibited. Fibres In the production of fibres, DMAc is used as a process solvent. It is recovered and recycled. The use of DMAc is very well controlled. This is also proved by the recovery process. In this process, DMAc is not seen as an intermediate. After removing of the solvent, it will end up in the waste streams, mostly after some cycles of reuse. Paint strippers This is a minor use and it is not supported by industry (the use is not registered). So far, we are not aware of this use with our customers but at this moment we cannot exclude it. This use is not mentioned in the current CSR as "uses advised against". We are also not aware of the conditions of this use. We will update our CSR so it will contain this use in the "uses advised against" section. A downstream user could always make his own risk assessment for this use, so a restriction could be a possibility to regulate this use.	
38	2012/09/19 13:46	Individual Italy	With reference to the draft proposal of ECHA to include the substance N,N-Dimethylacetamide (DMAC) in the draft list of the substances recommended for inclusion to Annex XIV for REACH authorization, we would point out the elements for exemption from REACH art. 58.2 for "industrial coatings" use, with specific reference to the case of the enamels for electrical wire insulation in the automotive division. According to Article 58.2 of REACH, uses or categories of uses may be exempted from REACH authorization requirement provided that the risks due to the property of the substance are properly controlled, on the basis of existing EU legislation imposing minimum requirements for the protection of human health or the environment. On the basis of Article 58.2 of the REACH Regulation, we submit that the use of DMAC for "industrial coating" (with specific reference to the case of the enamels for electrical wire insulation in the automotive division) should be exempted from REACH authorization for the presence of existing EU legislation, and in particular Directive 98/24/EC (CAD) on the protection of workers, Directive 2008/1/EC (IPPC) and Directive 2010/75/EC (IED) concerning the "integrated pollution prevention and control" which are existing EU legislation that properly control the risks to environment and/or the human health for this use.	**Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the Chemical Agents Directive. In relation to the Industrial Emissions Directive, please see response to comment #19 in Section I.

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			Indeed, Directive 98/24/EC is a Directive based on Article 118a of the EC Treaty, which provided for the adoption of minimum requirements in order to guarantee a better level of protection for the safety and health of workers and which allowed Member States to apply stricter (but not less stringent) requirements under certain conditions Within EU framework, a Community-level occupational exposure limit (OEL) value was established on the basis of Directive 2000/39/EC. Implementing such a limit is effective in limiting the risk to workers: OEL (EU): 10 ppm (36 mg/m3) as an 8 hour Time Weighted Average (TWA); 20 ppm (72 mg/m3) as a 15 min STEL. Note: skin Additionally a Biological Exposure Index (BEI) has been derived by the American Conference of Governmental Industrial Hygienists (ACGIH). The BEI provides a measure of total systemic exposure and is based on measurement of the DMAC metabolite monomethylacetamide (MMAc) in urine in end of shift samples. The BEI is 30 mg of MMAc/g creatinine. Ultimately the presence of the above mentioned existing EU legislation and exposure limits makes the risks of DMAC for "industrial coatings" properly controlled. . On the basis of the "Draft background document for N,NDimethylacetamide (DMAC)" of 20th June, it is also evident that the volume of DMAC used for "industrial coatings" is quite low because it's 3-5% of the total of the DMAC in the EU is used for "industrial coatings" (and so this specific case of enamels of magnet wire for the automotive division is also lower than the total percentage for "global" industrial coatings use) and so this specific case has a very low "contribution" to the total volume of DMAC, with the conclusion that impact of this use to the global risk of DMAC to human health and to the environment is very limited. Additionally it should be highlighted the lack of alternatives with lower hazard profile. In fact the alternatives for this specific use (as NMP) have the same hazard profile one of DMAC. So currently it's not possible to substitute DMAC with a substance with a lower hazard profile.	
36	2012/09/19 10:39	Company	we use this product(DMAC)as solvent in closed vessels to manufacture active products. there is no more residue in final product	Please see response to comment #4 in section I of this

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		France		document.
35	2012/09/19 01:03	Company Ireland	We request an exemption for the use of DMAc in the manufacturing of PVDF membranes under the condition that exposure levels during the manufacturing process are below those listed in the currently valid EU Regulation and the concentration of DMAc in the membrane is below 0.1 %. Dimethylacetamide (DMAc) is used as a solvent in the manufacture of a range of PVDF (polyvinylidene difluoride) micro-porous membranes. The DMAc solvent is critical in the process in order to achieve the desired membrane porous structure and performance characteristics. The DMAc solvent is extracted during the manufacturing process and previous testing has confirmed that DMAc is present only in negligible quantities (below 0.1 %) in the finished membrane. The membranes are utilised in a wide range of devices and applications some of which include; • Blood & plasma filtration • Disease screening • Filtration of parenteral solutions • Bulk filtration of pharmaceutical process streams Manufacture of these membranes is carried out in a tightly controlled GMP environment as well as ISO 9001 and ISO 13485 standards. As detailed above, the membrane is utilised in a variety of medical devices, some of which are required to be approved by the FDA. Some of the membrane is included in CE marked medical devices as per 93/42/EEC and for IVDs 98/79/EC. R&D work carried out to date has been unable to identify an alternative solvent that can be used to successfully manufacture equivalent membranes. The replacement of DMAc in the process with an alternative solvent may not be technically feasible. In case a suitable alternative will be identified, process re-development and qualification using an alternative solvent will require significant investment in time and resources in a multi-year program as these membranes are manufactured in a highly validated environment.	**Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the Chemical Agents Directive. In relation to the Industrial Emissions Directive, please see response to comment #19 in Section I. In relation to the Medical Devices Directive, please see response to comment #21 in Section I.

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			There is also a serious threat to the market as competitors based in the US would not need to comply with the authorisation for membrane manufacture outside the EU.. This causes an unfair burden on EU manufacturers due to increasing costs on membrane manufacture thus reducing economic viability. Exposure of workers: The risk of exposure of the operator whilst handling DMAc is low due to appropriate engineering controls (including containment, local exhaust ventilation (LEV)) and correct personal protective equipment (PPE)). Industrial hygiene monitoring is carried out on a regular basis to demonstrate that exposure levels are below the threshold limit value (TLV). A limit value is available for DMAC under the requirements of the Safety, Health and Welfare (Chemical Agents) Regulations 2001 and Directive 98/24/EC, This limit value is for an 8 hour OEL (10 ppm resp. 36 mg/m3) as well as a 15 minute reference period OEL (20 ppm resp. 72 mg/m3) so there is clear guidance available for safe working limits. Exposure to the environment/public: The waste DMAc from the process is primarily recovered for reuse in the manufacturing process, with the remainder disposed of in accordance with the site IPPC licence which places strict controls on emissions from the site (air, water and waste). From the IPPC Directive (2008/1/EC, Integrated Pollution Prevention and Control) arises the necessity for a company to have an Environmental Licence issued by the EPA, Ireland. Areas of use are equipped with spill barriers (bunded), containment programmes are in place as well as abatement systems.	
34	2012/09/18 21:54 See attachment *34_Comments CQ.doc*	CEPSA QUIMICA S.A. Company Spain	Large scale industrial uses, due to no risk has been identified for all DMAC uses (see attached document)	Thank you for your comment. As regards your proposal for restriction as an appropriate risk management for uses of DMAC associated with paint strippers, please see response to comment #42 in section I of this document. Please also note that the use of paint strippers containing DMAC below its Specific Concentration Limit (5%) is not in the scope of authorisation. This does however not necessarily apply for formulation of these mixtures.

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				See also response to comment #4 in section I of this document. In relation to the assessment of the wide-dispersiveness (# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in section I. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the Chemical Agents Directive and medicinal products legislation. In relation to the Pregnant Workers Directive, please see response to comment #21A in section I.
33	2012/09/18 21:44	European Federation of Pharmaceutical Industries & Associations International organisation Switzerland	Exemption from authorisation is requested for the use of N,N-Dimethylacetamide (CAS 127-19-5) 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 N,N-Dimethylacetamide (CAS 127-19-5) 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)	**Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the medicinal products legislation. **PPORD exemption request** As relates to your request for exemption for PPORD, please see response to comment #10 in section III.
31	2012/09/18 18:18	Company Switzerland	In all cases where PNEC or DNEC is available and will be relevant for handling of the substance of concern at industrial sites and the substance after the use is either transformed into another substance or will be treated as waste with due diligence, the risk to human health and the environment from the use of that substance can be considered as adequately controlled. As the use of N,N-dimethylacetamide (DMAC) as solvent solely at industrial	Regarding the request for exemption from authorisation, please note that industry's voluntary actions in reducing releases or related to the availability of alternatives cannot be considered as such as a reason to propose an exemption. In relation to the elements ECHA considers when deciding whether to include an exemption of a use of

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			sites will not lead to a wide-spread use of this substance, but the handling will be restricted on properly trained and authorised personnel handling the substance under strictly controlled conditions, we recommend to exempt the use of DMAC at industrial sites under strictly controlled conditions from inclusion in Annex XIV of the REACH regulation. The handling will be similar to that of transported isolated intermediates in accordance with REACH Article 18 (4) with the only deviation that DMAC that is used as a solvent will not be transformed into another substance. As DMAC that was used as a solvent may be recycled several times but will end up as waste and will be treated as such, we are convinced that an exemption from inclusion in Annex XIV can be justified in this case.	a substance in its recommendation, please see response to comment #33 in section I.
30	2012/09/18 17:07	Company United Kingdom	Uses (or categories of uses) to be exempted from the authorisation requirement: Exemption from authorisation is requested for the use of N,N-Dimethylacetamide (CAS 127-19-5) 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 N,N-Dimethylacetamide (CAS 127-19-5) 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 Art 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	**Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the Chemical Agents Directive and the medicinal products legislation. In relation to the Industrial Emissions Directive, please see response to comment #19 in Section I.

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			modified by the physical form. EU authorities (and other regulatory bodies throughout the world) evaluate the final medicinal product in conjunction with its entire production cycle. Thus these solvents are regulated by strict Pharmaceutical residual solvents guidelines. In addition, other existing EC regulation covers the risk management for solvents like DMAC. Hence, the use of DMAC in the production of API's or as analytical standards should be exempt from Authorisation. The relevant existing EC regulations are: Directive 2001/83/EC & Regulation (EC) No 726/2004 The use of N,N-Dimethylacetamide 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 concentration limit for N,N-Dimethylacetamide. Since the residual amount of N,N-Dimethylacetamide in the eventual product (drug substance) is safety-limited by the EMA (Guideline for Residual Solvents), in practice virtually all the N,N-Dimethylacetamide 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 N,N-Dimethylacetamide 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	

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			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) of this Directive and the volumes under Annex IIA (Thresholds and Emission Controls) 2000/39/EC Indicative OEL Values (for DMAC): The European Commission's committee, the Scientific Committee on Occupational Exposure Limit Values (SCOEL) advises on occupational exposure levels for chemicals in the workplace within the framework of Directive 98/24/EC on the protection of workers from chemical agents. Directive 98/24/EC requires the setting of indicative occupational exposure limit values (IOELVs). The EU sets non-binding, scientifically determined levels of exposure for particular chemical substances, below which workers will not experience detrimental effects to their health. These levels are then used by Member States to establish their own national limits. Due to SCOEL recommendation for the inclusion of DMAC in 1994, this resulted in DMAC being referenced in Directive 2000/39/EC. 2000/39/EC is the first list of IOEVLs in the implementation 98/24/EC. As the following safe limits have been set within EU law; 8 hour TWA: 10 ppm (36 mg/m^3), STEL (15 mins) : 20 ppm (72 mg/m^3). The use of DMAC can continue safely and be enforced without authorisation being necessary. 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.	

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29	2012/09/18 16:45	Association of the British Pharmaceutical Industry Industry or trade association United Kingdom	Uses (or categories of uses) to be exempted from the authorisation requirement: Exemption from authorisation is requested for the use of N,N-Dimethylacetamide (CAS 127-19-5) 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 N,N-Dimethylacetamide (CAS 127-19-5) 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 Art 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. EU authorities (and other regulatory bodies throughout the world) evaluate the final medicinal product in conjunction with its entire production cycle. Thus these solvents are regulated by strict Pharmaceutical residual solvents guidelines. In addition, other existing EC regulation covers the risk management for solvents like DMAC. Hence, the use of DMAC in the production of API's or as analytical standards should be exempt from Authorisation. The relevant existing EC regulations are:	**Article 2(5) exemption response** See response to Comment #33 in section I. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the Chemical Agents Directive and the medicinal products legislation. In relation to the Industrial Emissions Directive, please see response to comment #19 in Section I.

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			Directive 2001/83/EC & Regulation (EC) No 726/2004 The use of N,N-Dimethylacetamide 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 concentration limit for N,N-Dimethylacetamide. Since the residual amount of N,N-Dimethylacetamide in the eventual product (drug substance) is safety-limited by the EMA (Guideline for Residual Solvents), in practice virtually all the N,N-Dimethylacetamide 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 N,N-Dimethylacetamide 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	

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			covered under Annex I (Scope) of this Directive and the volumes under Annex IIA (Thresholds and Emission Controls) 2000/39/EC Indicative OEL Values (for DMAC): The European Commission's committee, the Scientific Committee on Occupational Exposure Limit Values (SCOEL) advises on occupational exposure levels for chemicals in the workplace within the framework of Directive 98/24/EC on the protection of workers from chemical agents. Directive 98/24/EC requires the setting of indicative occupational exposure limit values (IOELVs). The EU sets non-binding, scientifically determined levels of exposure for particular chemical substances, below which workers will not experience detrimental effects to their health. These levels are then used by Member States to establish their own national limits. Due to SCOEL recommendation for the inclusion of DMAC in 1994, this resulted in DMAC being referenced in Directive 2000/39/EC. 2000/39/EC is the first list of IOEVLs in the implementation 98/24/EC. As the following safe limits have been set within EU law; 8 hour TWA: 10 ppm (36 mg/m³), STEL (15 mins) : 20 ppm (72 mg/m³). The use of DMAC can continue safely and be enforced without authorisation being necessary. 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	

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			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 N,N-Dimethylacetamide, (CAS 127-19-5) 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	
26	2012/09/18 15:35	Company Gernmany	We request an exemption for the filling of DMAc from (intermediate bulk) container into small packages for lab use. The industrial packaging/filling for the lab use is done by well trained personnel and under the regime of 2000/39/EC (indicative occupational exposure limit values). All European countries have at least implemented the limit value of 2000/39/EC for DMAc in their national legislation. France has implemented an even lower value. Therefore, the risk for human health is considered to be acceptable based on workers' exposure. The use of N,N-dimethylacetamide as aprotic solvent in routine analytics, in lab synthesis and for testing of residual solvents is exempted from authorisation (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 DMAc usually refill DMAc 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 DMAc due to these uses. N,N-Dimethylacetamide is used for analysis of residual solvents according to Ph Eur (chapter 2.4.24) and USP (Chapter <467>) for headspace gas chromatography. Usually the volumes and the concentration of the substance are low. Additionally, the substance is classified as class 2 residual solvent in pharmaceutical synthesis (EMA/CHMP/ICH/82260/2006 ICH Topic Q3C (R5) Impurities). Therefore, the use of N,N-dimethylacetamide as analytical standard and for testing of residual solvents in pharmaceutical synthesis should be exempted	Thank you for your comment. 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 to 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. formulation of test kits or analytical standards with the intention to supply them for SRD purposes, would probably require authorisation. As regards processes such as refilling performed by manufacturers of a substance, whether they are in the scope of authorisation or not is an issue on which ECHA currently discusses with the European Commission. As soon as the issue has been clarified, ECHA will communicate the outcome on its website in the Questions & Answers section (http://echa.europa.eu/web/guest/support/faq/questions-and-answers-on-applications-for-authorisation).

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			from authorisation (scientific R&D) as well as packaging/filling for this use.	**Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the Chemical Agents Directive and the medicinal products legislation.
25	2012/09/18 15:12	CIRFS: European Man-made Fibres Association Industry or trade association Belgium	DMAC is identified as a Substance of Very High Concern (SVHC) according Article 57 c as it is classified in Annex VI, part 3, Table 3.1 of Regulation (EC) No 1272/2008 as toxic for reproduction 1B, H360D (May damage the unborn child), having an indicative occupational exposure limit (i-OEL) value and a skin notation according a first list of i-OEL as established in Commission Directive 2000/39/EU of 8 June 2000, in implementing amongst others Council Directive 98/24/EC. We are of the opinion that the REACH Regulation does not overrule the existing Dir 2000/39/EU. The Commission will ensure that all process steps of the Directive (see below) are implemented in its entirety in all member States. - Directive 98/24/EC proposes European objectives in the form of i-OEL for the protection of workers from chemical risks, to be set at Community level (and implemented via Dir 2000/39/EU). I-OEL are health-based, non-binding values, derived from the most recent scientific data available. - Although non-binding, Member States are required to establish a national occupational exposure limit value taking into account the Community limit value. According to our information there is only one Member State deviating, but by setting an even stricter value than the i-OEL value. - Member States shall bring into force the necessary laws, regulations and administrative provisions to comply with Directive 2000/39/EU by 31 December 2001. - Member States shall forthwith communicate to the Commission the text of those provisions and a correlation table between the provisions and this Directive. - Member States shall communicate to the Commission the text of the provisions of national law which they adopt in the field covered by this Directive.	**Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the Chemical Agents Directive.

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			Implementation of i-OEL, remains over the whole process under the control of the Commission. Any review of the i-OEL lists would be a Commission initiative. In the case of DMAC having an i-OEL with skin notation this has resulted in adequate control and protection (including skin protection) of the workers at industrial operations from chemical risks at Community level, which means that the Commission remains in charge. Based on this there is no need for authorization of DMAC within REACH, but should lead to an exemption for the use of DMAC at/in MMF operations.	
24	2012/09/18 15:02	DINOX Handels-GmbH Company Germany	The majority of DMAC imported by us is already covered by other European legislations (Pharma, Biocide). This industrial uses as well as the fibre uses are all strictly controlled uses. Too great an emphasis has been made of the minor uses. The whole process is based on the minority uses. This is absolutely inappropriate. WE SUPPORT THE RESTRICTION OF THE MINOR USES AND THE EXEMPTION OF ALL INDUSTRIAL USES.	**Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the medicinal products legislation. In relation to the Biocidal Products Regulation, please see response to comment #24 in Section I.
23	2012/09/18 14:48	Merck Sharpe & Dohme / Organon NV Company Netherlands	The use of DMAC as a solvent in the manufacturing of pharmaceutical ingredients and assocciated quality control applications should be exempted. Rationale for the Request for an Exemption as per Art 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. EU authorities (and other regulatory bodies throughout the world) evaluate the final medicinal product in conjunction with its entire production cycle.	**Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the medicinal products legislation and the Chemical Agents Directive. In relation to the Industrial Emissions Directive, please see response to comment #19 in Section I.

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			Thus these solvents are regulated by strict Pharmacutical residual solvents guidelines. In addition, other existing EC regulation is covering the risk management for solvents like DMAC. Hence, the use of DMAC in the production of API's or as analytical standards should be exempt from Authorization. The relevant existing EC regulations are: (i) CPMP/ICH/283/95 Residual Solvents Guideline: The use of solvents in Pharma production is regulated by the medicinal products directive, and there are specific limits provided under this regulation in the residual solvents guideline CPMP/ICH/283/95, for residuals in the drug. The use of solvents is covered specifically under the Pharmaceutical legislation with specific limits for specific substances referring to that guideline. (ii) 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) of this Directive and the volumes under Annex IIA (Thresholds and Emission Controls). (iii) 2000/39/EC Indicative OEL Values (for DMAC): The European Commission's committee, the Scientific Committee on Occupational Exposure Limit Values (SCOEL) advises on occupational exposure levels for chemicals in the workplace within the framework of Directive 98/24/EC on the protection of workers from chemical agents. Directive 98/24/EC requires the setting of indicative occupational exposure limit values (IOELVs). The EU sets non-binding, scientifically determined levels of exposure for particular chemical substances, below which workers will not experience detrimental effects to their health. These levels are then used by Member States to establish their own national limits. Due to SCOEL recommendation for the inclusion of DMAC in 1994, this resulted in DMAC being referenced in Directive 2000/39/EC. 2000/39/EC is the first list of IOEVLs in the implementation 98/24/EC. As the following safe limits have been set within	

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			EU law; 8 hour TWA: 10 ppm (36 mg/m³), STEL (15 mins) : 20 ppm (72 mg/m³). The use of DMAC can continue safely and be enforced without authorisation being necessary. In addition, there is existing regulation concerning the incineration of waste: (iv) 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	
22	2012/09/18 14:10	Individual Germany	As expatiated above, the industrial use of DMAc for development (PPORD) and production of polymer membranes does not need additional regulation and thus should not be subject to authorization requirements according to REACH. Nevertheless, if ECHA still sees the need for further regulation of DMAc in Europe a concentration limit for DMAc in the finished products would be an adequate and sufficient approach.	Thank you for your comment. Regarding your proposal for setting concentration limits in finished products as a more appropriate risk management option than authorisation, please see response to comments #8 and #24 in section I of this document. As to your request for exemption for PPORD, please see response to comment #10 in this section.
20	2012/09/17 22:51	EUROPACABLE Industry or trade association Belgium	Please find enclosed the position of the European WINDING WIRE Industry, expressed by the General Secretary of EUROPACABLE Winding Wire Group. SITUATION DMAC is used today (as well as NMP) as raw material for enamels in the high performance and high temperatures enamelled wires, above 200°C. That is 2% of the use of DMAC in EU. The European market of copper enamelled wires, 400 000 tons, for electrical motors and transformers, has been moving massively from the last decade, to this high temperature, with DMAC and NMP based enamels, coming from lower temperatures, without DMAC, nor NMP: More than 60% of wires have moved in Europe, to match the new efficiency requirements of electrical motors. Ecodesign and Industrial Directives are pushing in that way to save more and more electrical usage. PREPARATION OF ENAMELS	Thank you for your comment and the provided information. Regarding to your proposal for restriction as a more appropriate risk management option than authorisation, please see response to comment #8 in section I of this document. In relation to the assessment of the wide-dispersiveness (# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in section I. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in

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			4 Sites only in Europe are producing enamels for our industry. DMAC is handled in sealed circuits. All peripheral operations, as maintenance, are fitted with local equipment ventilation, high level protection equipments, in short time. They are severely controlled by local authorities. Example in France: Décret n°2009-1570 du 15 Déc. 2009. The typical measurements of exposure are 10 times under the limits. USAGE OF ENAMELS Enamels are directly introduced on the running wire, into the ovens. All 40 plants in Europe are fitted with recycling ovens and catalyst systems: this ensures 98% burned solvents –included DMAC- into CO^2 and NO^2. Thanks to this result, the WINDING WIRE industry discussed with EU a specific level of emission in the VOC Directive 1999/13/CE of 5 gr per kg of wire. The follow-up was in place in 1998. COMPETITION The 400 000 tons of enamelled wire used in Europe are produced in Europe, by more than 90%. Imports are 8%, and exports 12% outside EU. The trend to high temperature wires, initiated in Europe, is now largely followed all over the world. Restrictions of DMAC in Europe will distort the world competition. PROPOSAL The risk control level for Personnel exposure and for the environment, and the existence of legislations for Personnel exposure control as well as for the effluents to the environment, at the European level, leads us to ask that the use of the DMAC is excluded from the field of the authorization envisaged by the ECHA for this product, enamel of Winding Wire; this in application of the article 58 (2) of Reach. At least, we require the same evolution for DMAC, as NMP, corresponding to annex XVII of REACH. We want to find solutions in that way, and we ask to avoid the likely ban of DMAC in 2017, through annex XIV. Leonard DANEL	its recommendation, please see response to comment #33 in section I. This response also considers the Chemical Agents Directive. In relation to the Industrial Emissions Directive, please see response to comment #19 in Section I.

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			General Secretary of EUROPACABLE WINDING WIRE GROUP Diamant Building Boulevard Reyers Brussels BELGIUM	
19	2012/09/17 22:31	Company Ireland	The use(s) or categories of uses that are proposed to be exempted: Exemption from authorisation is requested for the use of N,N-Dimethylacetamide in the production of medicinal products as defined in Article 1(2) of the Directive 2001/83/EC relating to medicinal products for human use, as outlined in REACH Article 58(1)e. Exemption from authorisation is also requested for the use of N,N-Dimethylacetamide up to 10 tonnes/pa regarding Process Orientated Research and Development (PPORD) covering PPORD relating to production of medicinal products for human uses as outlined in REACH Article 56(3). 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 2000/39/EC Indicative OEL Values (for N,N-Dimethylacetamide) 2000/76/EC Waste Incineration Directive PLEASE SEE ADDITIONAL COMMENTS IN SECTION IV	**Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the medicinal products legislation and the Chemical Agents Directive. In relation to the Industrial Emissions Directive, please see response to comment #19 in Section I.
18	2012/09/17 18:26	Pharmachemical Ireland Industry or trade association Ireland	DMAC is used during the syntheses of active pharmaceutical ingredients as a solvent in a closed batch process. The manufacture of active pharmaceutical ingredients is performed within enclosed equipment in accordance with Good Manufacturing Practices (GMP). DMAC (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. Typically the handling, use and destruction of DMAC 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, • 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.	Thank you for your comment and the information provided. As regards the information on risks associated to your uses, on alternatives and socioeconomic considerations, please see response to comment # 41 in section I. Please see also response to comment #4 in this section. In relation to the assessment of the wide-dispersiveness (# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in section I. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding

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			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. In light of the above, exemption from authorisation is requested for the use of DMAC 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. The relevant existing EC regulations are: Directive 2001/83/EC & Regulation (EC) No 726/2004 1999/13/EC Solvent Emissions Directive 2000/39/EC Indicative OEL Values (for DMAC) 2000/76/EC Waste Incineration Directive	whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the medicinal products legislation and the Chemical Agents Directive. In relation to the Industrial Emissions Directive, please see response to comment #19 in Section I.
17	2012/09/17 17:14	B. Braun Avitum AG Company Germany	Use, that should be exempted: DMAC as solvent used for production of polysulfone membranes within a wet spinning process. Community legislation which is considered to justify the proposed exemptions: - German Occupational Safety and Health Act (regulation of production environment) - Medical Device Directive 93/42/EEC (regulation of finished medical device)	**Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the Chemical Agents Directive. In relation to the Medical Devices Directive, please see response to comment #21 in Section I.
12	2012/09/14 12:02	Company France	The use of DMAC in the wire enamels production process creates very limited exposure to the Personnel. It is used in a closed production process. Limited and short time exposure may occur during filter sockets change and sampling; in this case high level of inhalation and skin personal protective equipment is worn and adequate ventilation is implemented. DMAC has got OELs both short term and for 8 hours.	Thank you for your comment and the provided information. As regards the information on risks associated to your use, alternatives and socioeconomic considerations please see response to comment # 41 in section I.

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			We would like to stress especially for France that the exposure control of DMAC for the Personnel is implemented according to the Decree and Arrêté dated December 15, 2010. DMAC falls in the so called "substance à VLEP contraignante" list meaning OEL with mandatory status. Every year an exposure monitoring campaign is developed and realized by an Administration approved external Laboratory. In 2010 and 2011 the selected tasks, both short term and job monitorings, showed that exposure was each time less than the 10% of the OEL (without taking into account the personal protective equipment effect). These monitoring campaigns and results are shared with workers health and safety representatives (called CHSCT) and the Labour Inspector. Process atmospheric releases of solvents (including DMAC) are canalized and sent to an onsite incinerator which release limits are determined by the site permit to operate. This high level of product management is well described in the draft background document issued by ECHA date June 20, 2012 in the paragraphs "industrial coatings" page 4 and 7. Note that the enameled wire (typically copper wire with an enamel coating), considered as article according to Reach definitions contain less than 0.1% w/w of DMAC as shown in internal analytical results. This excludes any professional exposure after our direct customers production process and obviously for the customer. In line with the previous points we think that Art. 58(2) should apply and that the professional uses of DMAC should exclude DMAC of the authorization regime.	In relation to the assessment of the wide-dispersiveness (# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in section I. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the Chemical Agents Directive.
11	2012/09/13 11:58	Company Ireland	Exemption from authorisation is requested for the use of N,N-Dimethylacetamide (CAS 127-19-5) 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 N,N-	**Article 2(5) exemption response** See response to Comment #33 in section I. **Art 58(2) exemption response**

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			Dimethylacetamide (CAS 127-19-5) 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 Art 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. EU authorities (and other regulatory bodies throughout the world) evaluate the final medicinal product in conjunction with its entire production cycle. Thus these solvents are regulated by strict Pharmaceutical residual solvents guidelines. In addition, other existing EC regulation covers the risk management for solvents like DMAC. Hence, the use of DMAC in the production of API's or as analytical standards should be exempt from Authorisation. The relevant existing EC regulations are: Directive 2001/83/EC & Regulation (EC) No 726/2004 The use of N,N-Dimethylacetamide 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)	In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the medicinal products legislation and the Chemical Agents Directive. In relation to the Industrial Emissions Directive, please see response to comment #19 in Section I.

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			contains a specific concentration limit for N,N-Dimethylacetamide. Since the residual amount of N,N-Dimethylacetamide in the eventual product (drug substance) is safety-limited by the EMA (Guideline for Residual Solvents), in practice virtually all the N,N-Dimethylacetamide 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 N,N-Dimethylacetamide 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) of this Directive and the volumes under Annex IIA (Thresholds and Emission Controls) 2000/39/EC Indicative OEL Values (for DMAC): The European Commission’s committee, the Scientific Committee on Occupational Exposure Limit Values (SCOEL) advises on occupational exposure levels for chemicals in the workplace within the framework of Directive 98/24/EC on the protection of workers from chemical agents. Directive 98/24/EC requires the setting of indicative occupational exposure limit values (IOELVs). The EU sets non-binding, scientifically determined levels of exposure for particular chemical substances, below which workers	

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			will not experience detrimental effects to their health. These levels are then used by Member States to establish their own national limits. Due to SCOEL recommendation for the inclusion of DMAC in 1994, this resulted in DMAC being referenced in Directive 2000/39/EC. 2000/39/EC is the first list of IOEVLs in the implementation 98/24/EC. As the following safe limits have been set within EU law; 8 hour TWA: 10 ppm (36 mg/m³), STEL (15 mins) : 20 ppm (72 mg/m³). The use of DMAC can continue safely and be enforced without authorisation being necessary. 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 N,N-Dimethylacetamide, (CAS 127-19-5) 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	
10	2012/09/13		Exemption from authorisation is requested for the use of N,N-	Thank you for your comment.

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	11:51	Company Belgium	Dimethylacetamide (CAS 127-19-5) 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 N,N-Dimethylacetamide (CAS 127-19-5) 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 Art 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. EU authorities (and other regulatory bodies throughout the world) evaluate the final medicinal product in conjunction with its entire production cycle. Thus these solvents are regulated by strict Pharmaceutical residual solvents guidelines. In addition, other existing EC regulation covers the risk management for solvents like DMAC. Hence, the use of DMAC in the production of API's or as analytical standards should be exempt from Authorisation. The relevant existing EC regulations are: Directive 2001/83/EC & Regulation (EC) No 726/2004 The use of N,N-Dimethylacetamide 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	As regards the requested exemption for PPORD, we would like to make reference to REACH Article 55, in which the progressive replacement of SVHCs where this is technically and economically viable is mentioned as one of the objectives of authorisation. Therefore, we consider that 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. **Article 2(5) exemption response** See response to Comment #33 in section I. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the medicinal products legislation and the Chemical Agents Directive. In relation to the Industrial Emissions Directive, please see response to comment #19 in Section I.

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			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 concentration limit for N,N-Dimethylacetamide. Since the residual amount of N,N-Dimethylacetamide in the eventual product (drug substance) is safety-limited by the EMA (Guideline for Residual Solvents), in practice virtually all the N,N-Dimethylacetamide 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 N,N-Dimethylacetamide 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) of this Directive and the volumes under Annex IIA (Thresholds and Emission Controls) 2000/39/EC Indicative OEL Values (for DMAC): The European Commission's committee, the Scientific Committee on	

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			Occupational Exposure Limit Values (SCOEL) advises on occupational exposure levels for chemicals in the workplace within the framework of Directive 98/24/EC on the protection of workers from chemical agents. Directive 98/24/EC requires the setting of indicative occupational exposure limit values (IOELVs). The EU sets non-binding, scientifically determined levels of exposure for particular chemical substances, below which workers will not experience detrimental effects to their health. These levels are then used by Member States to establish their own national limits. Due to SCOEL recommendation for the inclusion of DMAC in 1994, this resulted in DMAC being referenced in Directive 2000/39/EC. 2000/39/EC is the first list of IOEVLs in the implementation 98/24/EC. As the following safe limits have been set within EU law; 8 hour TWA: 10 ppm (36 mg/m³), STEL (15 mins) : 20 ppm (72 mg/m³). The use of DMAC can continue safely and be enforced without authorisation being necessary. 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 N,N-Dimethylacetamide, (CAS 127-19-5) to be	

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			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	
9	2012/09/12 17:38	Industry or trade association United States	In consideration of the worldwide need for magnet wire with advanced insulations, NEMA urges that use of N,N-dimethylacetamide (DMAC) in the production of high-performance magnet wire (also known as winding wire) should be specifically exempted if ECHA insists on adding DMAC to the REACH Authorization List (Annex XIV). NEMA offers a similar proactive comment for 1-methyl-2-pyrrolidone (NMP) also.	Regarding your request for exemption, please see response to comment #31 in this section.
8	2012/09/12 17:29	Company United Kingdom	Exemption from authorisation is requested for the use of N,N-Dimethylacetamide (CAS 127-19-5) 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 N,N-Dimethylacetamide (CAS 127-19-5) 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 Art 58(2): EU authorities (and other regulatory bodies throughout the world) evaluate the final medicinal product in conjunction with its entire production cycle. Thus these solvents are regulated by strict Pharmaceutical residual solvents guidelines. In addition, other existing EC regulation covers the risk management for solvents like DMAC. Hence, the use of DMAC in the production of API's or as analytical standards should be exempt from Authorisation. The relevant existing EC regulations are: Directive 2001/83/EC & Regulation (EC) No 726/2004 The use of N,N-Dimethylacetamide 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	Concerning your request for exemption of PPORD, please see response to comment #10 in this section. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the medicinal products legislation and the Chemical Agents Directive. In relation to the Industrial Emissions Directive, please see response to comment #19 in Section I.

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			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 concentration limit for N,N-Dimethylacetamide. Since the residual amount of N,N-Dimethylacetamide in the eventual product (drug substance) is safety-limited by the EMA (Guideline for Residual Solvents), in practice virtually all the N,N-Dimethylacetamide 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 N,N-Dimethylacetamide 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. 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) of this Directive and the volumes under Annex IIA (Thresholds and Emission Controls) 2000/39/EC Indicative OEL Values (for DMAC): The European Commission's committee, the Scientific Committee on Occupational Exposure Limit Values (SCOEL) advises on occupational exposure levels for chemicals in the workplace within the framework of Directive 98/24/EC on the protection of workers from chemical agents. Directive 98/24/EC requires the setting of indicative occupational exposure limit values (IOELVs). The EU sets non-binding, scientifically determined levels of exposure for particular chemical substances, below which workers will not experience detrimental effects to their health. These levels are then	

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6	2012/09/12 12:52	Company Spain	Request for exemption from Authorisation for the use of N,N-Dimethylacetamide as a solvent in the production of medicinal products Background With ECHA's 4th recommendation published on 20th June 2012, the substance N,N-Dimethylacetamide (DMAC) was recommended for "prioritisation for authorisation". This solvent has an important role for the production of and as an analytical standard for medicinal products at Boehringer Ingelheim. Uses or Categories of Uses exempted Exemption from authorisation is requested for the use of N,N-Dimethylacetamide (CAS 127-19-5) in the production of medicinal products as defined in Art. 1(23) of the Directive 2001/83/EC relating to medicinal products for human use and 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 N,N-Dimethylacetamide (CAS 127-19-5) up to 10 tonnes/year regarding Process Orientated Research and Development (PPORD) covering PPORD relating to production of medicinal products for human and veterinary uses for pre marketing authorisation activities (clinical trials and manufacturing scale up)	**Article 2(5) exemption response** See response to Comment #33 in section I. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the medicinal products legislation and the Chemical Agents Directive. In relation to the Industrial Emissions Directive, please see response to comment #19 in Section I.

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			as outlined in REACH Art. 56(3) Within Boehringer Ingelheim, DMAC is used both in lab R&D scale and in the manaufacturing of Active Pharmaceutical Ingredients (APIs). For the production of pharmaceuticals, DMAC is one of a class of extremely useful solvents designated as polar aprotics to support reactions for producing intermediates and APIs. Rates and selectivity of certain reactions (e.g. nucleophilic substitutions) are substantially enhanced due to the solvent polarity and other properties. Polar aprotic solvents such as DMAC are essential for these reactions, since they prevent unreacted materials from being carried forward in the process stream, they minimise the formation of side products, and produce intermediates and APIs of the highest quality. In some cases, the properties of DMAC are unique in effecting a desired reaction reactivity, selectivity, solubility, or purification and no comparable performance with any other solvent is known or the alternative solvents pose a greater environmental, occupational health, or other concern. There are other polar aprotic solvents with similar physical or chemical properties (albeit of lower polarity) that could potentially be used in place of DMAC in some API manufacturing syntheses. The most common 'direct' alternative may be DMF (N,N-dimethylformamide). Others include formamide, N-methylformamide, N-methyl-pyrrolidone and N-methylacetamide. However, these alternatives carry essentially the same health hazard as DMAC. Most of these solvents are already on the REACH Candidate List or under Consultation for setting on the Candidate List. In addition, these solvents have lower polarity and for some purposes different reactivity; the replacement of DMAC with such solvents could lead to incomplete reactions and side products that impact the safety and quality of the API. Moreover, this would result in an increase in waste streams. At Boehringer Ingelheim the manufacture of APIs and associated intermediates are performed in enclosed reactor trains in accordance with Good Manufacturing Practices (GMP). DMAC (and other solvents) are introduced into the reactors via transfer systems designed to minimize environmental release, by trained personnel using appropriate engineering controls and/or protective equipment, and are thus contained within the process stream. Since the residual amount of DMAC in the product (drug substance) is safety-limited by the ICH Q3C (Guideline for Residual Solvents), in practice virtually all the DMAC used during manufacture would	

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5	2012/09/11 16:09	Company Germany	Request for exemption from Authorisation for the use of N,N-Dimethylacetamide as a solvent in the production of medicinal products Background With ECHA's 4th recommendation published on 20th June 2012, the substance N,N-Dimethylacetamide (DMAC) was recommended for "prioritisation for authorisation". This solvent has an important role for the production of and as an analytical standard for medicinal products at Boehringer Ingelheim. Uses or Categories of Uses exempted Exemption from authorisation is requested for the use of N,N-Dimethylacetamide (CAS 127-19-5) in the production of medicinal products as defined in Art. 1(23) of the Directive 2001/83/EC relating to medicinal products for human use and 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 N,N-Dimethylacetamide (CAS 127-19-5) up to 10 tonnes/year regarding Process Orientated Research and Development (PPORD) covering PPORD relating to production of medicinal products for human and veterinary uses for pre marketing authorisation activities (clinical trials and manufacturing scale up) as outlined in REACH Art. 56(3)	**PPORD exemption response** As regards your request for exemption of PPORD, please see response to comment #10 in this section. **Article 2(5) exemption response** See response to Comment #33 in section I. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the medicinal products legislation and the Chemical Agents Directive. In relation to the Industrial Emissions Directive, please see response to comment #19 in Section I.

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			It is important to avoid confusion between the mission of the Agency and the respective missions of the European Medicines Agency (EMA) 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. Therefore, Boehringer Ingelheim requests exemption from Authorisation for the use of N,N-Dimethylacetamide, (CAS 127-19-5) in the production and analytics of medicinal products (including the production of intermediates to manufacture active pharmaceutical ingredients for medicinal products) and associated PPORD activities.	
4	2012/09/11 10:51	Company Germany	Uses to be exempted The following uses should be exempted from the authorization requirement: 1) Industrial use as solvent in production of membranes for medical devices (regulated by Council Directive 93/42/EEC of 14 June 1993 concerning medical devices). 2) Use in PPORD for membranes of medical devices (regulated by Council Directive 93/42/EEC of 14 June 1993 concerning medical devices), up to 1 ton per year. The proposed exemption would concern approximately ten manufacturing sites and less than 1% of the total DMAC consumption in the EU. On the other hand the lifesaving treatment of more than 300,000 patients in the EU will be ensured. Existing Community legislation The professional use of DMAC is already regulated by the Community legislation on occupational health and safety, especially • COUNCIL DIRECTIVE 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work, • COUNCIL DIRECTIVE 92/85/EEC of 19 October 1992 on the introduction of measures to encourage improvements in the safety and health at work of pregnant workers and workers who have recently given birth or are breastfeeding, and	Regarding your request for exemption of PPORD, please see response to comment #10 in this section. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the Chemical Agents Directive. In relation to the Pregnant Workers Directive, please see response to comment #21A in section I. In relation to the Medical Devices Directive, please see response to comment #21 in Section I.

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			• COMMISSION DIRECTIVE 2000/39/EC of 8 June 2000 establishing a first list of indicative occupational exposure limit values in implementation of Council Directive 98/24/EC. Directive 98/24/EC "lays down minimum requirements for the protection of workers from risks to their safety and health arising […] from the effects of chemical agents that are present at the workplace" (Article 1). Risks to the human health are properly controlled by the included requirements, e.g. regarding determination and assessment of risks by the employer (Article 4), preference of substitution by non or less hazardous agents or processes (Article 6), obligations related to safe design, application of collective and individual protection measures (Articles 5, 6) as well as emergency preparedness (Article 7) and health surveillance (Article 10). Furthermore the protection of pregnant workers and the unborn child against chemical agents is explicitly addressed by COUNCIL DIRECTIVE 92/85/EEC, stipulating an assessment of the specific risks and the implementation of all necessary measures by the employer. In addition indicative occupational exposure limit values for DMAC are established on Community level by Directive 2000/39/EC thus representing binding minimum requirements for ensuring the protection of the health of workers at the workplace, against the risks arising from professional use of DMAC. Directive 2000/39/EC also addresses the general possibility of significant uptake of DMAC through the skin. Hence all significant exposure routes are taken into account and all resulting occupational risks are already adequately controlled. These are mandatory elements of the responsible employer's implementation of the above mentioned European legal requirements and the national transpositions in all Member States respectively. Compliance with these regulations and adherence to limit concentrations of DMAC is controlled by the competent authorities of the member states by means of inspections. Due to the nature of the manufacturing process for medical device membranes workers are not exposed to DMAC during production. The applied manufacturing processes also ensure, as required by the medical device legislation, that DMAC is not present in the finished medical devices (articles as defined by Art. 3/3 REACH). Already the DMAC content of the semi-finished products (membranes; articles as defined by Art. 3/3 REACH)	

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			is below 0.01 % w/w and thus irrelevant for any subsequent manufacturing steps. The concerned finished medical device products are regulated by strict Community legislation ensuring a high level of product safety and risk control: • COUNCIL DIRECTIVE 93/42/EEC of 14 June 1993 concerning medical devices. Risk control according 93/42/EEC ensures absence of any relevant hazardous substance or adequate risk reduction. The adequacy of the medical device legislation for risk control is evident in the REACH Regulation itself: • Article 60/2 and 62/6 REACH define that substance use in medical devices regulated under Directives 90/385/EEC, 93/42/EEC, or 98/79/EC is excluded from the authorization requirement if such substance has been identified for human health concerns only. This precondition applies to DMAC. NB: Due to the formal limitation of Articles 60/2 and 62/6 REACH on substance use IN medical devices it is necessary to include in Annex XIV the above proposed completive exemption for use in production / PPORD of medical devices. Compliance with medical device regulations is controlled by a notified body and subject to CE-marking regulations. Product and process oriented research and development (PPORD) Regarding the adequate regulation and risk control of DMAC use in PPORD by Community legislation, the same applies as pointed out for professional use in production. Additionally it should be taken into account that ensuring the high level of quality and safety of medical devices requires ongoing product and process oriented research and development. Currently no adequate less hazardous alternatives for DMAC are available or foreseeable. The requirement for a time and work intensive authorization process for DMAC in PPORD will significantly constrain the needed ongoing enhancement of the affected medical devices as well as medical innovation in Europe. The exemption for PPORD will prevent the discrimination against Research and Development sites in the European Union as well as decline of competitiveness of the affected European medical device manufacturers on	

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			the European and international market.	
3	2012/09/04 11:23	Company Germany	Sartorius Stedim Biotech GmbH proposes the Use of DMAc as a solvent for polyethersulfone membrane production by the precipitation bath process to be exempted from the authorization requirement. The membranes according to the below described process are used in pharmaceutical and food applications. Process description: The membrane forming polymer (e.g. polyethersulfone) and several process aids (e.g. pore forming agents) as well are physically dissolved in DMAc as the only solvent or the main component in a solvent mixture. No chemical reaction occurs during the preparation of the polymer solution. The viscous polymer solution is continually precipitated as a thin, liquid film in a non-solvent (precipitation bath) whereby the solid membrane forms with the desired structure and pore size distribution. As the liquid polymer solution is continually transported into the precipitation bath, the non-solvent mixture diffuses into the liquid film. When the miscibility gap of the polymeric solution is exceeded, the polymer precipitates forming a solid, highly porous, sponge like structured membrane. The solvent DMAc as well as the pore forming agents diffuse into the precipitation bath. The formed membrane is continually extracted in several extraction baths at ambient temperature. During extraction most of the residual solvents and process aids diffuse out of the membrane. In order to further remove residual solvents and process aids completely, the membrane is then continually washed with pure water in a washing cascade comprising several water tanks. Fresh water is added to the last tank and in counter flow principle flows down the cascade. During the extraction and washing steps the different process aids and solvent(s) are removed from the membrane, down to residual trace levels. At the end of the production process the membrane is dried and reeled up. Reasons for exemption The application of DMAc as a solvent in membrane production by the precipitation bath process represents a process, where a set of good practices is implemented that ensure the safety and health of the workers.	Thank you for your comment and the provided information. As regards information on the risks associated with your use, please see response to comment # 41 in section I. In relation to the assessment of the wide-dispersiveness (# of sites and potential for releases) of DMAC in the context of priority setting, please see response to comment #21A in section I. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the medicinal products legislation and the Chemical Agents Directive. The commenting party claims that '(…) the resulting membrane products are in compliance with the European Directives for use in pharmaceutical and food applications'. It is unclear from the comment which legislation in relation to food applications is being referred to.

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			The polymeric solution is prepared in enclosed vessels. DMAC is introduced into the vessel via transfer systems designed to minimise environmental release, by trained personnel using appropriate protective equipment. Casting of the viscous polymeric solution and transporting the liquid film to the precipitation bath occur in a closed system. The atmosphere is controlled until the cast film is quenched into the precipitation media, which is pure water. DMAc is completely water miscible and diffuses out of the forming membrane. During the extraction and subsequent washing steps DMAc is removed from the membrane down to residual trace levels below the concentration limit of 0.1% (w/w). The air concentration of DMAc during the process is below the threshold value of 36 mg/m³ or 10 ppm (TRGS 900 (DE)). The equilibrium Concentration of DMAc in the wastewater is below 0.5%. DMAc is readily biodegradable and digestible by activated sludge in biological wastewater treatment plants. The resulting membrane products are in compliance with the European Directives for use in pharmaceutical and food applications.	
2	2012/07/24 15:57	WeylChem Frankfurt GmbH Company Germany	The use of DMAC as a process solvent for chemical syntheses under strictly controlled conditions (complying with REACH article 18(4))should be exempted from restriction if the substance is included in Annex XIV. Under strictly controlled conditions exposure is minimised to a level where no relevant risk to workers and the environment is to expected.	Regarding your request for exemption, please see response to comment #31 in this section.

IV - Comments on uses for which review periods should be included in Annex XIV, including reasons for that:

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45	2012/09/19 21:46	Company Portugal	The changing of Fisipe plant to be compatible with other known solvent may required a lot of time. It is difficult to predict the time required for the changes because never occurred changes of solvent with acrylic fibre producers. The adequacy of the characteristics of the fibre to characteristics appreciated by Fisipe customers may require 2-3 years. The development of a new solvent may involve several years - we have no experience. Carry out tests at laboratory level and at pilot plant level is also estimated to be taking 3-4 years. We can admit that will be required more than 10-12 years (but we have no experience). This means that we need a review period longer than 10-12 years.	Please see response to comment #25 in this section.
41	2012/09/19 17:10	Federchimica Industry or trade association Italy	See above	Please see response to comment #25 in this section.
33	2012/09/18 21:44	European Federation of Pharmaceutical Industries & Associations International organisation Switzerland	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. EU authorities (and other regulatory bodies throughout the world) evaluate the final medicinal product in conjunction with its entire	**Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the medicinal products legislation and the Chemical Agents Directive. In relation to the Industrial Emissions Directive, please see response to comment #19 in Section I.

#	Date	Submitted by (name, Organisation/MSCA)	Comment	Response
			production cycle. Thus these solvents are regulated by strict Pharmaceutical residual solvents guidelines. In addition, other existing EC regulation covers the risk management for solvents like DMAC. Hence, the use of DMAC in the production of API's or as analytical standards should be exempt from Authorisation. The relevant existing EC regulations are: Directive 2001/83/EC & Regulation (EC) No 726/2004 The use of N,N-Dimethylacetamide 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 concentration limit for N,N-Dimethylacetamide. Since the residual amount of N,N-Dimethylacetamide in the eventual product (drug substance) is safety-limited by the EMA (Guideline for Residual Solvents), in practice virtually all the N,N-Dimethylacetamide 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 N,N-Dimethylacetamide 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.	

#	Date	Submitted by (name, Organisation/MSCA)	Comment	Response
			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) of this Directive and the volumes under Annex IIA (Thresholds and Emission Controls) 2000/39/EC Indicative OEL Values (for DMAC): The European Commission's committee, the Scientific Committee on Occupational Exposure Limit Values (SCOEL) advises on occupational exposure levels for chemicals in the workplace within the framework of Directive 98/24/EC on the protection of workers from chemical agents. Directive 98/24/EC requires the setting of indicative occupational exposure limit values (IOELVs). The EU sets non-binding, scientifically determined levels of exposure for particular chemical substances, below which workers will not experience detrimental effects to their health. These levels are then used by Member States to establish their own national limits. Due to SCOEL recommendation for the inclusion of DMAC in 1994, this resulted in DMAC being referenced in Directive 2000/39/EC. 2000/39/EC is the first list of IOEVLs in the implementation 98/24/EC. As the following safe limits have been set within EU law; 8 hour TWA: 10 ppm (36 mg/m^3), STEL (15 mins) : 20 ppm (72 mg/m^3). The use of DMAC can continue safely and be enforced without authorisation being necessary. 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	

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			values to both air and water	
30	2012/09/18 17:07	Company United Kingdom	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 N,N-Dimethylacetamide, (CAS 127-19-5) 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.	**Article 2(5) exemption response** See response to Comment #33 in section I. **Art 58(2) exemption response** In relation to the elements ECHA considers when deciding whether to include an exemption of a use of a substance in its recommendation, please see response to comment #33 in section I. This response also considers the medicinal products legislation.
25	2012/09/18 15:12	CIRFS: European Man-made Fibres Association Industry or trade association Belgium	Some specific characteristics of MMF have already been mentioned in section 2. Transitional arrangements. The textile fibre supply chain is a very complex supply chain. MMF production is at the beginning of this supply chain and changes at the beginning have consequences for all subsequent stages. Some man-made fibres have been using DMAC for decades, and over that period several fibre properties have been improved to result in better end-use products. It is very unlikely that the same properties will be achieved in a very limited time period. Many studies on alternatives have been carried out (long-ago and reviewed), and no new information in the search for alternatives is to be expected. See also Section 1 part 3. In the search for alternatives, MMF is depending on new solvents introduced by the chemical industry. Supposing the chemical industry is successful, the lead time to	Thank you for your comment. Please note that setting 'upfront' review periods[2] for any uses requires that the Agency has access to adequate information on different aspects relevant for a decision on the review period. ECHA currently assessed that the information available is not sufficient to conclude upfront on specific review periods. Therefore, ECHA did not propose such review periods. It is to be stressed that all authorisation decisions will include specific review periods which will be based on concrete case specific information provided in the applications for authorisation.

[2] i.e. review periods already included as entry in Annex XIV and not decided upon, case by case, on the basis of information becoming available in the authorisation application phase of the process.

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			develop a substance which has also an economical viable potential is estimated to be 3 to 4 years. Testing as alternative for MMF at laboratory level and at pilot plant level is also estimated to be taking 3 to 4 years. Approval may start during the pilot plant phase, but will certainly run out for the high tech applications by at least 2 years. Construction or rebuilding of a MMF production plant could be done within two years, but heavily depending on the scope or reconstruction. This all results in a lead time of 10 to 12 years before a new solvent with improved health properties, and giving similar fibre properties at an economical feasible price would be completely implemented. As mentioned earlier, based on past testing and evaluation of alternatives, the chance that this will happen are quite small, and based on the above considerations MMF is asking for a review period of at least ten years.	
4	2012/09/11 10:51	Company Germany	time frame for medical devices The high level of safety and regulation required for development and production of medical devices within Europe requires time and cost intensive research, development and risk control, including clinical trials. Production processes and equipment are highly specialized and customized hence requiring prolonged planning, implementation and installation time. Current state-of-the-art membrane technologies require approximately 20 years between first research and development and the broad use of a new technology. These conditions should be carefully assessed and taken into account when deciding on general and individual review periods.	Thank you for your comment. Please see response to comment #25 in this section. Furthermore, note that guidance on the type of information in an application for authorisation which may impact the review period when granting authorisation can be found in the *Guidance on the preparation of an Application for Authorisation* (http://echa.europa.eu/documents/10162/13637/authorisation_application_en.pdf), as well as in the *Common approach for evaluation of applications by RAC and SEAC* (http://echa.europa.eu/documents/10162/13555/common_approach_rac_seac_en.pdf).