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Responses to Comments Document (RCOM) on ECHA's Draft 5th Recommendation for N,N-dimethylformamide (DMF) (EC number: 200-679-5)

This document provides ECHA's responses to the comments received during the public consultation on the draft 5th recommendation for inclusion of substances in Annex XIV of REACH, which took place between 24 June and 23 September 2013. In addition to this Response to Comments table, on ECHA's website there are available zip-file(s) including all attachments to the individual comments (as far as not confidential):
http://echa.europa.eu/addressing-chemicals-of-concern/authorisation/recommendation-for-inclusion-in-the-authorisation-list/previous-recommendations/5th-recommendation (see column "Additional documentation" in substances' table)

PUBLIC VERSION

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ECHA
EUROPEAN CHEMICALS AGENCY

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
2488	2013/09/23 23:23	essenscia, Industry or trade association, Belgium	Industrial process solvents like DMF are the backbone of chemical and pharmaceutical industry. They are often used at conditions that are similar to intermediate chemicals (chemical synthesis, chemical extraction processes, etc.). The use of DMF in consumer products is restricted according to Annex XVII of REACH (restriction 30). Manufacturers outside the EU and companies importing manufactured products into the EU would not be affected by the authorisation requirements, which could lead to a permanent competitive disadvantage for EU industry. Authorisation requirement for a safe industrial process solvent use is disproportionate. As DMF is a chemical agent, employers have to take measures to protect workers according to the Chemicals Agents Directive (CAD). If ECHA and Member States have concerns on the exposures of workers, national CAD enforcement is in place and can enforce companies, instead of using the costly and unsecure authorisation regime. In general, we'd like to express our concern on how the score for the prioritisation and especially the 'wide dispersive use' factor has been calculated (draft background document on DMF of 24 June 2013 point 3.1 Prioritisation). Wide-dispersive uses are characterized by use(s) of a substance on its own, in a preparation or in an article at many places (sites) that may result in significant releases and exposure to a considerable part of the population (workers, consumers, general public) and/or the environment. This means that uses taking place at many places, which however do not result in significant releases of a substance, may be considered only as 'wide-spread' but not as 'wide-dispersive' (as stated in ECHAs General Approach for Prioritisation of Substances of Very High Concern (SVHCs) for Inclusion in the List of Substances Subject to Authorisation of 28 May 2010 page 5). So the factor should not only be	Thank you for your comment. **Permanent competitive disadvantage and proportionality of the authorisation process** REACH is an EU Regulation aiming to ensure a high level of protection of human health and the environment while enhancing competitiveness and innovation. There is a strong societal interest to protect humans from risks potentially arising from uses of substances toxic to reproduction, e.g. DMF. Authorisation is not comparable to a ban or restriction of a substance but rather to a requirement to request authorisation for carrying out particular uses with the substance. The obligation to apply for authorisation is to ensure that risks are properly controlled or that socio-economic benefits are outweighing the risks, while concomitantly it is a strong incentive to search for and develop suitable alternatives. We fully acknowledge that the supply of DMF as a substance or in mixture to general public is not allowed and the CAD obligations apply to DMF. This is the case for all substances classified as R1A/B and these substances are also covered by Title VII of REACH. Although subjecting DMF to authorisation may have an impact on individual companies in their capacity as manufacturers of DMF the companies 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. To the extent DMF may be

			based on the number of sites, but also on a more realistic scoring of potential exposure. The background document mentions only "For some operations significant potential for workers exposure cannot be excluded" without specifying the concerned operations. The registration dossier mentions only industrial uses and a professional use in laboratories, where no significant release is taking place. The used PROCs and ERCs in the registration dossiers could be used as an indication for exposure. There should also be a bigger difference in the weighting factors between the industrial, professional and consumer uses where consumer uses in general entail a more wide dispersive use. Wide dispersive use (WDU) score of 9 was given by ECHA based on DMF. This has been practically simply concluded from high tonnage assumed to be equivalent to a high number of sites and high release. This is neither true nor appropriate. Sites and use are very different factors: 1) Most of the sites are rather laboratories using DMF in their Research analytics. As research use is exempted from authorization laboratories should be excluded for the prioritization scoring. 2) Most of the DMF tonnage is used at a small number of sites (e.g. chemical synthesis). Consequently, to classify number of site as medium is more appropriate 3) Only industrial uses are registered apart from Laboratory use (An example for professional use is research in universities).This implies clearly a non-wide dispersive use. This is also reflected in the ERCs 4) Again as only industrial uses are registered one can assume that emission control is in place as this is mandatory according to EU legislation already. Consequently, DMF release has to be classified as insignificant or non-diffuse/controlled . Consequently overall score should have been: (IP (inherent properties) = 0) + (V (volume) = 9) + [(Sites = 2-3) * (Release = 1)]. This leads to an overall prioritization score of 11/12 instead of 18 and another ranking of the batch of prioritised SVHC.	present in imported articles ECHA shall investigate if this poses a risk it shall propose a restriction on these articles as per Article 69(2) of the REACH Regulation. It is acknowledged that the users of DMF in the EU would have somewhat higher costs than their competitors outside the EU if they need to get an authorisation. This cost increase depends on the application fee and, in particular, the costs of preparing the application. ECHA has taken steps to see to it that the application process is predictable and proportionate by giving information and guidance on its website (http://echa.europa.eu/web/guest/applying-for-authorisation). This is to support the applicants to focus their applications and thus reduce the application costs. For instance, for threshold substances, ECHA's Risk Assessment Committee (RAC) has produced "reference DNELs" which help the applicants to understand how the Committee will determine if risks are adequately controlled. This will focus the preparatory work and thus reduce the application costs. ECHA has also informed on its website the length of the review periods that its Socio-economic Analysis Committee (SEAC) would propose to the Commission in its opinion. This is normally seven years, but a long review period of 12 years is possible, too. Market certainty among potential applicants is thus increased. The overall aim is to facilitate a proportionate and efficient application process so that the exposure to humans and the environment relating to the use of substances of very high concern is minimised while maintaining the competitiveness of the EU industry. Furthermore, in the registration dossiers manufacturers and importers are already required

				to describe how the exposure of workers is controlled. Thus, if the chemical safety report is well prepared during the registration phase the applicant would not need to carry out additional work during the application process. The authorisation application and decision making process involves a systematic scrutiny of applications. This scrutiny by RAC and SEAC covers also the risk management measures and the resulting exposure levels as identified and estimated by the applicant. Furthermore, the Commission can impose additional conditions as part of the authorisation decision. Hence, the authorisation process as whole involves an additional guarantee that the risks of the substances of very high concern are properly controlled. Please also note that companies can apply in a flexible manner either alone or as groups. This can also be done by suppliers in one go for all their clients that use a substance in a similar manner. Finally, the overall impact of the authorisation requirement depends on the share of (the application cost for) DMF in the total production cost. Usually the share of raw materials (in comparison to capital and labour costs) is relatively low. If this is the case also for DMF, the overall cost increase would be relatively low and the effect on the competitiveness of the industry using DMF in the EU would be relatively low, too. In line with the objectives of REACH, the system (first inclusion in the candidate list, secondly inclusion into Annex XIV, third application and granting of authorisation) was set up to provide a clear long-term incentive for companies to substitute substances of very high concern. However, the substitution should take place only when an available safer alternative is technically and economically feasible. Uses of substances applied for can continue after the set "sunset date" has expired, where the Commission has granted an

				authorisation, which is to be expected in cases where applicants have made a good case. **Prioritisation** *General consideration* ECHA has the legal obligation to recommend substances included in the Candidate List for inclusion in Annex XIV to the European Commission at least every second year. According to Art 59(1) the Candidate List is established for eventual inclusion in Annex XIV. Prioritisation is a task of comparing those substances included in the Candidate list to determine which one would be included first. The workability of the authorisation process justifies the need for a gradual inclusion of substances in Annex XIV. Substances not prioritised remain on the candidate list and will be considered for their priority in the later recommendation. The prioritisation approach applied by ECHA was discussed with the Member State Committee and has been agreed by this Committee. Please refer to the description of the prioritisation approach (http://echa.europa.eu/documents/10162/17232/axiv_priority_setting_gen_approach_20100701_en.pdf) It is noted that all priority setting approaches are conventions on how to systematically use the information available on the chosen or given prioritisation criteria (i.e. how to weight and combine the criteria in qualitative and/or quantitative terms). To draw overall conclusions there is a need to integrate complex bits of all relevant kinds of information. Therefore the assignment of weighting factors and scores remains to be done by expert judgement. In case of the applied prioritisation approach this has been done in discussion with the MSC. *Scoring volume* According to the agreed prioritisation approach the assessment of the "volume" criterion for DMF has been based on the complete annual volume

				supplied in the EU to uses not exempted from the authorisation requirement. The assessment of the "wide dispersive use" criterion is carried out independently from the assessment of the volume criteria. *Scoring WDU* With regards the justification as to why DMF is considered as wide-disperse, according to the agreed prioritisation approach, the assessment and scoring of the 'wide-dispersive use' criterion is broken up in the two sub-criteria 'Site-#', which is basically the number of sites where the substance is used, and 'release' which describes the releases in terms of pattern (where relevant) and amount versus anticipated risk. As for volume, the wide-dispersiveness is assessed for the substance taking into account all uses within the scope of authorisation (i.e. not only whether one use could be regarded as wide-dispersive). - *'Site-#'* As stated in the background document based on the available information ECHA has assessed that DMF is used as solvent in uses not exempted from the scope of authorisation by industrial end-users spread across several industrial sectors representing in total more than 100 sites of potential exposure (e.g. chemical, pharmaceutical, agrochemical, textile, electronic and gas sectors). Comments received during public consultations from different sector associations provide evidence to support this statement (as for the chemical sector, although sites where DMF is used in SRD are not considered in the assessment, there are also sites using DMF in manufacturing or production processes). - *'Release'* Note that the fact that the substance is used at more than 100 sites entails by itself the exclusion of score '0' (insignificant release) for the release

				criteria according to the prioritisation approach. Deciding about assigning a score '1' or '3' for a particular substance does not comprise an exposure or risk assessment, but making a rough evaluation of its use pattern relying on some basic indicators. As the purpose is just to compare substances, it is not so important where the exact (arbitrary) borders between '1' and '3' are set, but rather the criteria to be consistent for all substances assessed. ECHA has been (especially since registration data is available) mainly relying on the process types involved in the overall uses of a substance, often reflected by the PROC use descriptors (or ERC, when the main concern is environmental exposure). Those reflect normally key-information on operational conditions and engineering controls to be expected. ECHA has also been using further indicators, as part of the weight of evidence assessment, especially for substances neither used in processes with clearly very high release potential nor used solely in closed-systems. However, for such use patterns a 'release' score '1' was assigned normally only in specific cases such as: where strict RMM is a clear requirement already due to the nature of uses (e.g. use along with radioactive materials, use in clean-room conditions for electronics etc.) and provided there are not significant professional or consumer uses; concentrations (in substance/mixtures/articles) are for all uses very low; frequency and duration are clearly very low due to the nature of use (e.g. contact with vehicles' tyres by professionals); properties of the substance indicate both low fugacity (e.g. low volatility) and low dermal absorption potential. It is noted that assessment of information that normally requires higher level of assessment (detailed operational conditions, correctness of reported in CSR exposure/risk assessment,

				available measurement data, appropriateness / reasonability of recommended RMM) is beyond the scope of this step of the authorisation process. Similarly, registration and accordingly implementation by downstream users of appropriate RMM is anyway a requirement for the hazardous substances, including those in the Candidate List – while information on the actual implementation of appropriate RMM across the supply chain is missing or not possible or necessary to assess at this stage of the process. The main concerns that had triggered a release scoring '3' for DMF had been the following: (i) Registration data indicated that the substance is used at industrial sites in systems where potential for significant exposure arises (e.g. PROC 4, PROC 5, PROC 8a). Transfer (e.g. manual discharge), mixing (potentially in open or semi-open systems) and industrial cleaning operations were identified as carrying the most significant potential for exposure. Moreover, no substantial information was available with respect to process descriptions / operational conditions or potential for exposure for further confirmed uses of DMF (e.g. use in electronic industry and formulation). (ii) Formulation of mixtures had been registered; however no substantial information was available on their types and use pattern. Type of mixtures reported in Annex XV dossier included paints, coatings, adhesives, mastics, sealants, binding agents, finishes and compounds and corrosion inhibitor product(s). Uncertainties on the use of DMF in strippers and in epoxy inks by the aerospace industry were stressed. Uses of such mixtures were considered as of potential relevance for industrial workers and possibly for professional workers. However, as documented in the prioritisation table and background document, ECHA has acknowledged that according to

				registration data such use of DMF by professionals should not occur. In other words, the information on potential uses is only reflecting uncertainties in the use patterns. (iii) It had also been noted that DMF, although having a relatively low to medium vapour pressure at room temperature, it is readily absorbed via all exposure routes (including via skin) Comments providing information on uses were received also during the current public consultation, with the representativeness depending widely on the sector of use. Regarding mixtures, a few individual companies provided some information on the use, in their facilities, of some industrial mixtures mentioned above (e.g. mixture used in coating, finishes, as corrosion inhibitor), claiming that it occurs under controlled conditions. No information has been received with regard to the specific use pattern of sealants in the Aeronautic. Uses in strippers (and apparently also in epoxy inks) in the EU have not been confirmed or excluded. Regarding the main sectors of use (Chemical, pharmaceutical, agrochemical, textile), the overview-comments received reflected a situation similar to what was summarised in the background document; and claiming that there is no continuous exposure of workers to DMF. The main processes appear to take place either in enclosed reactors or in semi-closed system (equipped with exhausted ventilation) and being largely automated; while exposure appears to rather be limited to operations such as control, transfer/loading, maintenance or cleaning. Here it is noted that the frequency of such operations is apparently sector and company specific but in absolute terms, taken into account also the diversity of sectors/uses and the high number of sites at which DMF is used, it appears not to be justified to regard the frequency of

				exposure as negligible. Based on the above, ECHA considers that the initially assigned score '3' for release is justified for DMF.
2473	2013/09/23 19:31	ChemSec, International NGO, Sweden	ChemSec supports the listing and prioritisation of this substance to the Authorisation list (Annex XIV) due to its wide dispersive use and high volumes. Wide dispersive use: DMF is used as a solvent in synthesis of chemicals and in particular as solvent in the production of artificial leather and polyurethane coated textiles, in the electronic industry, but has also other uses as gas stabiliser and intermediate. It is also used as laboratory chemical and at many industrial sites with high share of downstream users. DMF is known to be water soluble solvent that is easily absorbed via all exposure routes. The highest dispersive exposure in process uses is associated with mixing and industrial cleaning operations with high workers exposure potential. It is used in a lot of industrial sites. It is expected that a high volume of similar articles containing DMF is imported in the EU. However there is no information on SVHC in imported articles notifications according to Art 7.2 of REACH available on the ECHA webpage (the official SVHC listing took place on 19 December 2012). High volumes: DMF is manufactured / used in high volumes (up to 100.000tonnes per year). The substance should therefore be prioritised for listing in Annex XIV on this basis.	Thank you for your support and for giving your reasoning.
2464	2013/09/23 18:27	DMSO Producers Association, Industry or trade association, United States	The main long-term alternative to DMF available on the market is dimethylsulfoxide (DMSO). Whilst DMSO certainly is not a drop-in substitute for all applications, it has a broad spectrum of uses in which it could replace DMF, with significantly reduced environment and/or health risk. - There is an extensive physico-chemical, environmental and toxicological database available on DMSO demonstrating that DMSO is of low concern for the environment and the human health. (SIDS dossier available at: http://webnet.oecd.org/Hpv/UI/SIDS_Details.aspx?id=4	Thank you for the information. Information regarding availability of alternatives is important information for inclusion in authorisation applications by companies. Availability of alternative is 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. Note that the application for authorisation process

			C5A1A36-54BC-41C3-950F-AE4171BDA7F5, REACH dossier available at: http://apps.echa.europa.eu/registered/data/dossiers/DISS-828e0a4f-03e4-1d1a-e044-00144fd73934/DISS-828e0a4f-03e4-1d1a-e044-00144fd73934_DISS-828e0a4f-03e4-1d1a-e044-00144fd73934.html As a result, DMSO is not classified as hazardous according to the principles of Regulation (EC) N° 1272/2008. - DMSO, like DMF, belongs to the class of aprotic polar solvents. It is a powerful organic solvent which is well established in the industry, with dissolving properties for binder polymers (including PVDF, PAI, PUs, acrylics, ..) identical to DMF. - DMSO is widely available. Arkema manufactures DMSO in Europe. Three other manufacturers, Gaylord (USA), Toray (Japan) and Hubei Xinfa (China) have registered DMSO (REACH registration number 01-2119431362-50-0000). Global DMSO manufacturing capacity is estimated to be 100,000mT. DMSO has a very low level of corrosivity. Plant experience has shown that more than a 10-year life can be expected with stainless steel equipment under continuous exposure to DMSO-water solutions. DMSO does darken considerably when exposed to mild steel, copper, brass, lead or zinc for long periods. Therefore, if color and purity are prime considerations, 304 or 316 stainless steel or aluminium are recommended metals of construction. To prevent DMSO from freezing (melting point 18°C), a stainless steel coil is usually installed in storage tanks to keep the contents between 40° and 50°C. Hot water is suggested for circulation through the coil. Provisions should be made for tracing all pipe lines which carry anhydrous DMSO. Alternatively, adding the liquid of low freezing point to DMSO is used in order to lower a freezing point. In fact, an industrial grade DMSO including water is commercially available. In conclusion, although corrosivity and freezing point are issues to be taken into consideration when designing a DMSO based chemical processing plant, DMSO is already an established industrial solvent in the chemical, pharmaceutical and textile industries.	includes also a public consultation, for collecting relevant information on alternative substances or technologies by third parties. Therefore, in case the substance is included in Annex XIV, you will have the possibility to provide such information for the uses applied for authorisation.
2462	2013/09/23	Company, Portugal		-

	18:21			
2456	2013/09/23 17:42	Company, Ireland	We request that the use of DMF in the manufacturing of pharmaceutical products be exempted from authorisation. We are part of the ChemLeg Pharmaceutical companies network which wrote a collective comment to the public consultation. This comment is attached here and has also been submitted through the European Federation of Pharmaceutical Industries and Associations (EFPIA).	Thank you for your comment. **Exemptions** As regards your request for exemption please note that uses (or categories of uses) can only be exempted from the authorisation requirement on the basis of Art 58(2) of REACH, unless they are already explicitly exempted in REACH Art 2(5 or 8) or in Art 56 (3-6). *Exemptions based on existing legislation* According to Article 58(2) of REACH it is possible to exempt from the authorisation requirement uses or categories of uses "*provided that, on the basis of the existing specific Community legislation imposing minimum requirements relating to the protection of human health or the environment for the use of the substance, the risk is properly controlled*". ECHA considers the following elements when deciding whether to include an exemption of a use of a substance in its recommendation: - There is existing EU legislation addressing the use (or categories of use) that is proposed to be exempted. Special attention has to be paid to the definition of use in the legislation in question, compared to the REACH definitions in accordance with Art. 3(24). Furthermore, the reasons for and effect of any exemptions from the requirements set out in the legislation have to be assessed; **-** This EU legislation properly controls the risks to human health and/or the environment from the use of the substance arising from the intrinsic properties of the substance that are 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 lifecycle 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, it is considered that: (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 and/or 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. 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 based on the determination and assessment of risk and general principles for the prevention of risk, associated with hazardous chemical agents. CAD (through Directive 2009/161/EU) establishes indicative occupational exposure limit values for DMF. In addition, CAD

[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.

				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 DMF from authorisation in accordance with Article 58(2) REACH Regulation. 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 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 DMF from authorisation.

				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. The Directive encourages substitution/reduction in usage of organic solvents and sets down emission limit values for particular activities (including manufacturing of pharmaceutical products; certain coating activities) to protect human health and the environment. Under Article 58 IED Directive, volatile organic compounds (VOCs) such as DMF 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 DMF 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 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 activities listed in Annex VII (such as in pharmaceutical manufacturing; certain coating activities) 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. More generally, IED Directive requirements apply to specified chemical industry activities (Annex I) such as production on an industrial scale of pharmaceutical products including intermediates; organic chemicals; and plant protection products or biocides. Annex II contains an indicative list of the main polluting substances and includes large groups of substances. The directive does not specify how to identify polluting substances for which a permit for an installation needs to include an emission limit value. For these reasons the substances for which the minimum requirements set out in the directive apply are not specified in a way that would allow the use of the IED Directive as a reason for exemption under Article 58(2) REACH. It is further noted that pursuant to Article 62(5)(b)(i) REACH an applicant may justify in his authorisation application that emissions from an installation for which an IPPC-permit has been granted do not need to be considered when deciding on an authorisation. This implies that a case specific consideration is needed to judge whether risks arising from IPPC installations are properly controlled. 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 DMF. Therefore, they may be not regarded as a sufficient basis for exempting uses of DMF from authorisation in accordance with Article 58(2) of the REACH Regulation. *PPORD exemption request* 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 any further PPORD activities which may require the use of a substance included in Annex XIV should in principle aim at developing alternative substances and technologies to replace the SVHC in question or to further develop processes to improve the control of risks until feasible alternatives are available. However, ECHA notes that actors can apply for a use of a substance (included in Annex XIV) for any PPORD activity and the pertinence of a PPORD activity with a substance identified as SVHC should be justified in an authorisation application and be scrutinized and decided in the authorisation granting process in accordance with Article 60. *Use exempted according to REACH Art 2(5 or 8) or in Art 56 (3-6)* As a general remark, please note that individual companies may benefit from the exemptions foreseen in REACH Art 2(5 or 8) or in Art 56 (3-6) if the conditions are met. According to Art. 2(5) substances used in medicinal products for human and veterinary use within the scope of the relevant EU legislation are exempted from the authorisation process. *Other reasons to justify exemption*

				Information and concerns brought forward in your comment, e.g. on availability and suitability of alternatives, socio-economic benefits of continuing 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 not relevant to a request for exemption according to Art. 58 (2). Such information is however important and can be included in the application, in case you decide to apply for authorisation of your uses of the substance or if your supplier applies for you. 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)).This information as well as any other use and user specific conditions 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. Note that 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 properly controlled or that there are no alternatives available and the socio-economic benefits are outweighing the risks arising from the uses. **DMF use pattern in specific industrial sectors/companies** It should be considered that the inclusion in Annex XIV is per substance and not per (sector specific) uses. Therefore screening in the prioritisation phase does not assess the volume, number of site

				or exposure levels from single uses or categories of uses, but aims to deduce whether the substance as a whole fulfil the prioritisation criteria. 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. Please also refer to response to comment 2488 (sub-title "prioritisation" for further justification of the WDU scoring). **Added value of the authorisation process** Please refer to response to comment 2340.
2455	2013/09/23 17:38	European Diagnostic Manufacturers Association (EDMA), Industry or trade association, Belgium	General comments on the recommendation to include the substance in Annex XIV, including the prioritisation of the substance: The European Diagnostic Manufacturer's Association (EDMA) would like to comment on the prioritisation of N,N-Dimethylformamide (DMF) for possible inclusion in Annex XIV of Regulation 1907/2006/EEC (REACH). EDMA requests ECHA to recommend against inclusion of DMF on Annex XIV and instead consider other risk management options for DMF as part of the class of polar aprotic solvents, for the following reasons: • The IVD sector uses only small quantities of DMF under strictly controlled industrial and laboratory conditions; • Substitution is challenging and might be considered possible only for another polar aprotic solvent which is already listed as a substance of very high concern; • Both application for Authorisation and actual substitution would be burdensome for our industry which is more than 90% SME– seeking substitution would impact hundreds of IVDs on an individual basis, triggering extensive and complex re-validation and re-registration processes for each assay. Use and exposure:	Thank you for your comment. **No alternatives / Socioeconomic benefits of use / Impacts of ceasing use / Low risks** Topics such as the availability and suitability of alternatives, socio-economic considerations regarding the benefits of a use or the (adverse) impacts of ceasing a use as well as information on the low level of risk associated to a use are important. Information regarding these topics should be provided as part of the application for authorisation (e.g. in the analysis of alternatives, the chemical safety report or the socio-economic analysis). This information will be taken into account by the Risk Assessment and Socio-Economic Analysis Committees when forming their opinions and by the Commission when taking the final decision. It may impact the decision on granting the applied for authorisation and the conditions applicable to the authorisation, such as e.g. the length of the time limited review period of the authorisation. However, it is to be stressed that the prioritisation

			In vitro diagnostic medical devices (IVDs) provide medically useful diagnostic information by examination of a specimen derived from the human body. The IVD industry contributes a fraction of the total use of DMF in the EU. Of the total EU volume (10,000 – 100,000 t/y), the IVD sector use is under 15 t/y, or < 0.15%. DMF is used in the manufacture of IVDs, both as a process chemical and as a component of the final product. This submission focusses on the use of DMF as a process chemical (given that IVDs have an exemption from the requirement to apply for Authorisation where DMF is a component of the final product). EDMA notes that Authorisation could however affect supply of DMF for use in the final IVD. Known as a 'universal solvent', DMF is used in diverse IVD technologies including manufacture of synthetic chromogenic substrates, synthetic diagnostic peptides, diagnostic dyes, conjugates and dissolution of stabilizers used in IVDs. Using synthetic antibodies or synthetic antigens instead of living, actively infectious antigens means running a diagnostic test without risk of infection. DMF is one solvent in a class of solvents called 'polar aprotics'. Other aprotic solvents include N-methylpyrrolidone (NMP), N,N-dimethylacetamine (DMAc), N,N-dimethylacetamide, and dimethylsulfoxide (DMSO). They are solvents that dissolve both polar reactants (such as ions) and nonpolar compounds (such as hydrocarbons). Polar aprotics are also miscible in a wide range of organic solvents including water. These two properties of DMF - ability to dissolve polar reactants and miscibility with water - are the key to the role of DMF in IVD reagents. DMF is required to solubilize small polar molecules called "coupling agents" which link antibodies to other proteins (enzymes used in the detection systems of diagnostic products). At the same time, the proteins being linked (or "conjugated") are soluble in water. DMF provides an environment in which the polar coupling agents are dissolved and can actually link the aqueous proteins. The REACH Descriptor Process categories which best describe the use of DMF in the manufacture of final IVDs and components used in IVDs are 'PROC 15 – Use as a	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/docu+E2ments/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. Note also that 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 properly controlled or that there are no alternatives available and the socio-economic benefits are outweighing the risks arising from the uses. **Intermediate status** Regarding the use descriptors that apply to describe your use, it seems that you refer to PC19 – use as intermediate. If it is the case, please carefully assess that the use of DMF in the production of final IVD devices and components used in IVD fits with the definition and interpretation of the intermediate status. According to Appendix 4 of the "Guidance on intermediates" (http://echa.europa.eu/documents/10162/13632/intermediates_en.pdf) from December 2010, "An isolated intermediate (i.e. a substance "used […] in order to be transformed into another substance"), is used in the manufacturing of another substance where it is itself transformed into that other substance. […] Whenever a substance (A) used in a chemical processing is not used in the manufacturing of

			laboratory reagent', PROC 3 –Use in closed batch process (synthesis or formulation) and PROC 19 – Intermediate. This is a consequence of the small quantities involved at the workplace. DMF is used under closed processes or in fume hoods with no or minimum exposure to the worker and environment well under the indicative occupational exposure limit for DMF set by Directive 98/24.EC. This limited exposure meets the requirements of national legislation such as COSHH in the UK or Ireland's Control of Substances Hazardous to Health Regulations 2003. National legislation follows Community legislation relating to Workers' health legislation: Chemical Agents Directive 98/24/EC, Carcinogens and Mutagens Directive 2004/37/EC and Council Directive 92/85/EEC. In the wider industry, DMF is used not only in the manufacture of IVDs but also manufacture for: • Research and development products manufactured under laboratory conditions and where the final product does not contain DMF. These end products are used by cancer research institutes, medical research organisations, universities and pharmaceutical companies to investigate cellular disease processes, with a view to developing better diagnostic tools, pharmaceuticals and therapies; • Non-IVD industries producing commercially marketed diagnostic tests for forensic or veterinary purposes. Substitution: Due to its unique properties, it would be difficult or impossible depending on the assay in question, to substitute DMF for another polar aprotic solvent. DMF offers sufficient solubility of many inorganic reagents (e.g. salts, acids & bases) to facilitate chemical reactions that would not be feasible or robust in many other organic solvents. While the possibility for substitution cannot be ruled out, trials already performed within the industry have reported lack of success. As noted in the ECHA background document, safer alternatives are not available. The only possible substitute in an IVD would be another polar aprotic solvent of sufficient strength and characteristics– however these have the same intrinsic properties with respect to reproductive toxicity.	another substance (B) in order to be itself transformed into that other substance (B), it is necessarily used in order to achieve another function than transformation, either as part of the manufacturing of another substance (B) (e.g. as catalyst, processing agent, solvent), or as part of another activity (e.g. as an individual step in the production process of an article). While this other function may still involve chemical modification of the substance (A) used in the process, this type of use cannot be considered as the manufacturing of another substance (B) from the transformation of substance (A). Therefore, as soon as the main aim of the chemical process is not to transform a substance (A) into another substance (B), or when substance (A) is not used for this main aim but to achieve another function, substance (A) used for this activity should not be regarded as an intermediate under REACH." **Security of supply** Good communication in the supply chain is essential to decide the most appropriate actor(s) to apply for authorisation. This can be manufactures/importer(s) covering their customers' uses; or any downstream user(s) in the supply chain covering their own use, their suppliers' placing on the market and/or their customers' uses; or any combination of these which best meets the needs of the specific supply chain. For a downstream user who wishes to continue a use and apply for authorisation but is concerned about supply (e.g. concerned that the suppliers in EU will cease manufacture/import), there is also the possibility to consider importing the substance and submitting (in case required, see guidance above) a registration themselves. Please also refer to responses to comments 2427 (other RMO), 2456 (exemption based on existing legislation) and 2488 (permanent competitive

			Footnote 3 in the Background Document for DMF notes that the lack of availability of substitutes was not taken into account for prioritisation of DMF for potential inclusion on Annex XIV. At the same time, application for Authorisation necessitates testing to find substitutes where possible. EDMA points out that a regulatory measure to prioritise DMF for Annex XIV is particularly inappropriate when the only potential alternatives are other polar aprotic solvents. Without alternatives, our only options as an IVD Industry would be to repeatedly apply for Authorisation – a costly and resource-intensive exercise as is explained below – or exit the market for valuable but lower revenue generating products or move manufacturing out of the EU. A different risk management option which does not force substitution should be found which regulates uncontrolled exposure of all polar aprotic solvents rather than providing a different regulatory solution for each substance. Application for Authorisation would mean conducting studies to see whether or not substitution is possible. Because each IVD assay is performed for different analytes on different biological human samples for different sensitivity and specificity parameters, candidate substitutes would need to be tested for on an assay-by-assay basis. It would necessitate extensive studies to screen candidate replacements to ensure no change in product performance – in particular sensitivity and specificity testing. Without sufficient testing, the risk arises to have either false negative or false positive tests, which has tremendous and possibly fatal consequences for patients and the health of the population. Should an appropriate substitute be found, the next step would be re-validation testing performed on an assay-by-assay basis. Re-validation means: • Testing of large populations of patients to ensure rare variations in the blood proteins of some patients would not interfere with the safe diagnostic performance of the test, leading to potentially fatal consequences for the individual patient, e.g. in a malaria or gonorrhoea test; • Full stability trials on 3 lots of the reformulated component to ensure the replacement did not adversely impact the products' shelf lives. In many cases,	disadvantage and proportionality of the authorisation process).

			accelerated stability tests will neither be practicable nor possible necessitating real time tests which may result in additional chemical wastes and delays in product availability of 1-2 years. Without a stable IVD with shelf life which lasts months or even years, diagnostic tests cannot be manufactured centrally and transported across the healthcare market in Europe and globally; • Relicensing in certain markets both EU and non-EU, leading to protracted introduction time and a complex implementation pathway for the products; • The huge cost to IVD products for validation and registrations could mean decisions to remove some products from the market or manufacture outside EU; • Considerable time and resources to implement a portfolio re-design per impacted product diverted from re-investment into further innovation in diagnostic testing. Application for Authorisation would necessitate the IVD industry checking if substitution is possible. This check would necessitate the extensive sensitivity, specificity and stability testing described above. Therefore the application for Authorisation itself would be a significant burden on our industry which would potentially be prohibitive, jeopardizing the supply of IVDs for health institutions, blood banks and patients. Furthermore, IVD manufacturing is impacted during this same timeline by the proposed prioritisation of 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-OPnEO) which, if listed on Annex XIV, would considerably increase the complexity and time needed to address identification of substitutes and redesign products. In some cases, both (sets of) substances are included in the manufacture or formulation of the finished IVD products. It is not feasible for one industry to plan for the substitution of multiple different substances that are used in IVDs on the basis that global supply of these devices must be maintained and where validation processes (if viable alternatives exist) are estimated to take up to 10 years for a single substitution. The complexity of preparing for several substitutions would significantly impact the IVD industry. Distortion of EU market and disproportionate impact on SMEs: As over 90% of the European IVD industry is made up of	

			SMEs, the disproportionate cost of applying for Authorisation and in particular the necessity to divert R&D resources into seeking substitution –would fall on those least able to pay for it. Suppliers may choose not to apply for Authorisation in order to market the relatively small volumes of DMF used by the IVD industry, the amount of material being too small to justify the cost. The cost of application could fall wholly on the IVD industry. Authorisation would affect the ability of European companies to compete in our own market. Third country manufacturers exporting IVDs into Europe and using DMF as a process chemical would be unaffected by the Authorisation requirement. Europe has a strong IVD manufacturing base however this measure could encourage manufacturing to move outside of the EU. It is important that the healthcare industry continues to have access to DMF at rates determined by the market in order for Europe to maintain its leadership in healthcare innovation. Any substitution (if possible) would trigger re-validation and re-registration of hundreds of products. The €10.8 billion market revenue generated by the European IVD industry only makes up 0.8% of total health care expenditure in the EU (2011 figures), however Member States could see costs rise considerably or access to new innovative products disrupted regardless if Authorisation is granted or a substitute is found. Because re-validation/verification and re-registration would be required for impacted IVDs the substitution requirements of authorisation would hit SMEs disproportionately, affect the competitiveness of European IVD manufacturing and impact on the availability and cost of diagnostic medical products. The cost and resources needed for re-validating/verifying hundreds of IVDs manufactured in Europe due to the use of relatively small quantities of DMF – for which the only substitute would be another polar aprotic solvent – seems disproportionate indeed to the intended policy outcome which is to manage the exposure risk to worker health and safety. This is already strictly controlled in IVD manufacturing under laboratory conditions and according to EU and national legislation governing exposure of dangerous chemicals. Given the hugely	

			positive impact which the use of DMF has for diagnostics and healthcare and the lack of feasible alternative for a non-SVHC substance, EDMA requests that ECHA find a different risk management option for DMF and indeed for the group of polar aprotic solvents.	
2453	2013/09/23 17:29	CORONET SPA, Company, Italy	The Coronet Spa opposes the authorization process for the DMF because no other chemical can be used in our work cycle. the Coronet spa produces synthetic leathers and uses the DMF for dissolving the polyurethane. The production process involves coagulation and splamatira; in the clotting process the wash water is recovered and sent to a distillation process in which the DMF is recovered totally, in the process of coating the fumes generated are convoglaiti within scrubber to be washed with water deminaralizzata. waters obtained are conveyed to a distillation for the recovery of DMF. The DMF is used for industrial purposes. Our processes and protection measures are in accordance with EC legislation, as required by Directive 2009/161/EC and 1999/13/EC standard. within the workplace can not access pregnant women workers.	Thank you for your comment. Please refer to response to comment 2455 (no alternatives) and 2456 (DMF use pattern).
2449	2013/09/23 17:05	Company, Germany	We ask ECHA to recommend against inclusion of DMF in Annex XIV and instead consider other risk management options for DMF as part of the class of polar aprotic solvents. DMF is used in the manufacturing and/or as part of in vitro diagnostic medical devices (IVDs). As a diagnostics company we are part of the European Diagnostics' Manufacturer's Association (EDMA)- EDMA has submitted on our behalf a paper to the public consultation. This comment is attached hereafter and has also been submitted by EDMA.	Thank you for your comment. Please refer to response to comment 2455 (EDMA).
2448	2013/09/23 17:02	Vetex n.v., Company, Belgium	Same approach for all aprotic solvents needed: Like most of the aprotic solvents, DMF is classified as a reprotoxic substance (Rep. Cat. 1B). At this moment, different aprotic solvents (DMF, NMP, DMAC) are treated in a different way under REACH. Some are considered under the restriction procedure (e.g. NMP), others are proposed to be handled under authorization (DMF, DMAC). However there is no scientific logic to handle very similar solvents under different regulatory approaches. Both the industry and many authorities are the opinion that it would be more logical and consistent to treat all aprotic solvents in an identical way (e.g. all under restriction).	Thank you for providing your opinion. Please refer to responses to comments 2427 (consistent approach with similar solvent), 2456 (DMF use pattern) and 2488 (Scoring WDU).

			Prioritization score does not reflect real use in textile coating: The management of Vetex n.v. can't share the high prioritization score ECHA's draft recommendation (dated 24th of July 2013) calculated for the inclusion of DMF in the Authorization list. The use of DMF in the textile coating industry is not characterized as being wide-dispersive. In the textile coating industry DMF is only used in an industrial setting under controlled conditions (environment and protection for worker exposure). In order to minimize the emissions to the environment below the emission limits the substance DMF is treated in a incinerator at 830°C – 850°C. This technology warrants the strict emission limits imposed by the directives are met. Use to be considered wide-spread instead of wide-dispersive: Wide-dispersive uses are characterized by use(s) of a substance on its own, in a preparation or in an article at many places (sites) that may result in significant releases and exposure to a considerable part of the population (workers, consumers, general public) and/or the environment. This means that uses taking place at many places, which however do not result in significant releases of a substance, may be considered only as 'wide-spread' but not as 'wide-dispersive'. With regard to the textile coating, there are a limited number of sites with controlled emissions below the emission limits. Risk management measures are in place to control workplace exposure and emissions to the environment. Hence the management of Vetex n.v. cannot agree that a score of 9 is given to "wide dispersive use". As release is controlled (meaning releases at the workplace may occur but that risk management measures are in place to control workplace exposure) the score 1 should be applied for "release", giving an overall score of 3 for "wide dispersive use". This results in a total score of 12 for prioritization, instead of 18 as concluded in the draft background document for DMF.	
2441	2013/09/23 16:23	DINOX Handels-GmbH, Company, Germany	a) Aprotic solvents, such as DMF should be exempted from the authorisation process under the provisions of Art. 58.2 [on the basis that existing legislation already imposes minimum requirements	Thank you for providing your opinion. Please refer to responses to comments 2456 (exemption), 2427 (other RMO), and 2455 (No alternative).

			relating to the protection of human health or the environment for the use of the substance]. DMF has a defined safe level (threshold). b) AUTHORISATION IS NOT THE MOST APPROPRIATE OR EFFICIENT PROCESS TO MANAGE THE MAJOR SOURCES OF RISK IN THE USE OF DMF. The majority of DMF is used in industrial situations under controlled conditions posing no health risk to workers. This has already been communicated by several companies for the SVHC public consultation. As proposed by several users and producers, we also propose to restrict the consumer use, whereas all other industrial uses are either already covered by other community regulations/legislations or are handled under strictly controlled conditions. Still the justification for the inclusion of DMF into Annex XIV is only the listing as a CMR substance. This risk however is not evident by companies with experience in handling DMF for more than 20 years and longer, as you can see in your list of comments on the Annex XV dossier. There are no alternatives with a lower hazard profile. Similar solvents have the same CMR rating and are not are real alternative. Several users have clearly stated that they have tested alternatives in the past, but have not found one that is really suitable due to different reasons. Finally we are wondering, what comments is ECHA looking for, if all the given comments on the Annex XV dossier are not relevant and may only become so at a later stage? What is the aim of this public consultations?	**Restrict consumer use** Note that DMF is already restricted for the general public according to the generic entry 30 of Annex XVII of REACH Regulation for reprotoxic substances when the individual concentration is equal or above to the applicable generic concentration limit according to the CLP Regulation nr. 1272/2008/CE as substance, as constituent of other substance or in a mixture (Note the changes applicable to the generic concentration limit as of 2015 for reprotoxic substances). **Aim of the public consultations (SVHC Annex XV and A.XIV recommendation)** On the aim of the public consultations (PC) at the different steps of the authorisation process, and the information sought, please see http://echa.europa.eu/web/guest/addressing-chemicals-of-concern/authorisation/public-consultation-in-the-authorisation-process In brief, at the SVHC PC it is mainly aimed to receive information on whether the substance fulfils the SVHC criteria, as well as use and tonnage information to support the later prioritisation task. At the A.XIV Recommendation PC, information is sought on the prioritised substances, mainly on uses which should be exempted, as well as information regarding the complexity of supply chain (relevant for allocating the substances to the different 'latest applications date lots'). Comments on the priority as such are also welcome thereby. However, as prioritisation is not a Yes/No assessment for inclusion to A.XIV, but rather a comparison of substances in the Candidate List for including the most relevant ones first (a certain number of substances each time, depending on the anticipated capacity of ECHA to handle applications), removing a substance from a draft recommendation is foreseen only in cases where

				the respective information leads to a significant and factual change regarding the tonnage of the substance expected to be in uses in the scope of authorisation. Finally, at the PC at the application-for-authorisation phase information on potential alternative substances or technologies is sought.
2434	2013/09/23 15:51	EFPIA, Industry or trade association, Belgium	Introduction: The EU Pharmaceutical Industry's Chemical Legislative (ChemLeg) Working Group (Abbott/Abbvie, AstraZeneca, Bayer, BMS, Boehringer-Ingelheim, Eli Lilly, GSK, Janssen Pharmaceuticals (Companies of Johnson and Johnson), Merck, MSD, Novartis, Novonordisk, Pfizer, Roche, Sanofi, Sandoz -each of them are members of EFPIA) requests that the use of DMF in the manufacturing of pharmaceutical 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 is exempted from REACH authorisation requirements. This exemption would also include all PPORD uses of DMF (up to 50ts/pa) in the production of medicinal and veterinary products. We believe this exemption should be granted because of the following key reasons: • Community Legislation relating to the Health, Safety and Environmental (HSE) control of DMF already exists in particular community legislation relating to Occupational Exposure Levels. ChemLeg members have DMF OEL monitoring data taken from various Active Pharmaceutical Ingredient (API) Manufacturing facilities across various Member States which can be shared with ECHA on request from ECHA; • Community Legislation covering substitution/replacement of DMF already exists under the Industrial Emissions Directive; • Use of DMF in pharmaceutical manufacturing is not wide dispersive • If technically possible at all (see reasoning below), DMF can only be substituted by other Aprotic Solvents with similar health hazards;	Thank you for providing your opinion. Please refer to response to comment 2456.

			• Substituting a solvent used in the manufacture of a commercially available Pharmaceutical Product may require additional human and animal testing (contrary to the principles of REACh); • Substituting a solvent used in the manufacture of a commercially available Pharmaceutical Product requires the current Marketing Authorisations (granted by the European Medicines Agency (EMA)) to be amended leading to excessive costs (3M – 12M EUR per product) and time delays; • REACH article 62(5)(b)(i) suggests that an Annex XIV listed substance handled in a facility that is permitted by Directive 96/61/EC doesn't need to consider risks from Human Health or the Environment when submitting an application for an Authorisation Use of that Substance The amount of DMF manufactured and/or imported into the EU is, according to registration data, in the range of 10,000 – 100,000 t/y. No information on exports is provided. According to registration information complemented by information from industry consultations performed in 2011 and 2012 (Annex XV report, 2012; RCOM, 2012), 50% of the total volume (5,000-50,000 t/y) is used in the production of APIs or crop protection ingredients. The majority of the uses take place at industrial settings. There is no registered use for consumer products (ECHA Draft Background Document for DMF June 2013). Within the EU Pharma Industry, DMF is used at Bulk API Manufacturing Sites (there will be some use at small R&D facilities but these volumes of DMF are limited). According to the DG ENTR website, there are approx. 900 Bulk API Manufacturing sites across the EU-27 (http://ec.europa.eu/enterprise/sectors/healthcare/competitiveness/importance/facts-figures_en.htm). In creating this consultation response, the Pharmaceutical Industry's Chemical Legislative Working Group accounted for 60 Bulk API Manufacturing sites of which 30 use DMF; extrapolating that data to the data on DG ENTRs website and we get a maximum of 450 individual Bulk Manufacturing Sites using DMF (or approx. 15 sites per Member State). DMF is used within the ChemLeg Group of companies	

			under highly controlled conditions in batch production processes (which typically are run a few times per year/month at most pharmaceutical plants) and is therefore not considered as wide dispersive use nor is there a continuous potential for exposure. Benefits of Aprotic Solvents (such as DMF) in the Production of Medicinal Products DMF is an aprotic solvent used to manufacture Active Pharmaceutical Ingredients (APIs) for pharmaceutical products which treat potentially life threatening or debilitating conditions such as, Small Cell Lung Cancer, Cervical Cancer, Herpes Simplex virus, Varicella Zoster viruse, asthma, eczema and psoriasis. DMF is also used in Pharmaceutical lab R&D and as an analytical standard for a number of medicinal products. The powerful solvating properties of Polar Aprotic Solvents (such as DMF) facilitate organic synthesis reactions which often, cannot be achieved in less polar solvents. Polar Aprotic Solvents offer general high solubility of many APIs and intermediates which often have poor solubility in less polar solvents. This also facilitates processes that require minimal solvent quantities, compared with the much larger volumes of other solvents that may be required. 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 DMF are essential for these reactions, since (a) they prevent unreacted materials from being carried forward in the process stream and (b) they minimise the formation of side products, thereby producing intermediates and APIs of the highest quality. There are other Polar Aprotic Solvents with similar physical or chemical properties (albeit of lower polarity) that could potentially be used in place of DMF in some API manufacturing syntheses. The most common 'direct' alternative may be DMAC. Others include formamide, N-methylformamide, NMP, NEP and N-methylacetamide. However, these alternatives carry essentially the same health hazard as DMF. Some of these solvents are already on the REACh Candidate List or have been proposed to Annex XIV or Restriction. In addition, these solvents may have different reactivity and so the replacement of DMF with such solvents could lead to	

			incomplete reactions and side products that impact the safety, quality and yield of the API. Moreover, this may result in additional animal and human testing and waste streams. In other cases, the properties of DMF are so unique in effecting a desired reaction reactivity, selectivity, solubility, or purification that no comparable performance with any other solvent is known or the alternative solvents pose a greater environmental, occupational health, or other concern. Scoping work to identify alternatives to DMF in the manufacture of pharmaceutical products within the EU has been undertaken in the past with very limited success. Significant development work would be required to identify and validate viable alternatives involving major changes to the manufacturing processes and the Marketing Authorisation (see below). Given the complexity of global supply chains, the ability of the pharmaceutical industry to secure a continuous supply of medicines to the market could be at risk if DMF was not available for use. Description of the Use of DMF in the Production of Medicinal Products The manufacture of APIs and associated intermediates are performed in enclosed reactor trains in accordance with Good Manufacturing Practices (GMP). DMF (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). Residual amounts of DMF in the eventual pharmaceutical product are safety-limited by the ICH Q3C (Guideline for Residual Solvents). So in practice, virtually all the DMF used during manufacture would be present in the waste streams (other than that lost through evaporation) which is primarily disposed of via incineration (some recycling of DMF will occur). Altogether, the risks of environmental exposure of DMF in the pharmaceutical manufacturing environment are minimized by the equipment design and operational controls.	
2431	2013/09/23	GIFAS, Industry or trade	Please refer to attached document	Thank you for your opinion.

	15:37	association, France		Please refer to comment 2427 (other RMO) and 2455 (no alternative).
2427	2013/09/23 15:14	Finland, Member State	We agree that DMF appears to meet the priorisation criteria for inclusion in Annex XIV. The provided information indicates that in most identified uses human exposure seems to be controlled in reported conditions of use and with existing RMMs. At some stages in industrial processes worker exposure potential cannot be excluded and there are uncertainties. One concern seems to be potential exposure to DMF from imported articles. Risks caused by uses of DMF are difficult to assess at this stage of the priorisation process. We have some reservation regarding the use of authorisation (Annex XIV) as a risk management measure for DMF. Currently, it is not clear whether authorisation is the most appropriate risk management route. To our understanding in some uses it is very difficult to substitute DMF (e.g., manufacture of active pharmaceutical ingredients) and alternatives or techniques for these uses are currently not known. Furthermore, many other available aprotic solvents have similar hazardous properties as DMF (e.g. DMAC and NMP). From a risk management point of view polar aprotic solvents should be treated in as consistent way as possible. For one aprotic solvent, N-methylpyrrolidone (NMP), a proposal for restriction is currently under evaluation in ECHA and it can provide valuable information on how to choose risk management measures for aprotic solvents. In addition, discussions in the Commission with regard to DMAC (included in ECHA`s 4th recommendation for substances for inclusion in Annex XIV) can provide further advice on selection measures also for DMF. The criteria in article 58(3) are used to define the order for selecting priority substances from the candidate list to be included in Annex XIV. Despite of the fact that a priorisation criterion does not mention assessment of the most appropriate risk management option during the	Thank you for your comment. **Other RMO / consistent approach with similar solvents** As acknowledged in your comment, the prioritisation for the inclusion in Annex XIV is based on the criteria set out in Art 58(3) and follows the approach described in the agreed general approach document. In the process of assessing whether a substance on the Candidate List has priority for inclusion in Annex XIV and therefore should be recommended for inclusion in this annex ECHA is not in the position to assess the pertinence of alternative regulatory risk management options for the substance or some of its particular uses. In accordance with REACH Article 59 it is at the discretion of the Member States and the European Commission to decide for which substances Annex XV dossiers with proposals for identification as SVHC are subjected to the SVHC identification process. As you reflect, ideally considerations on the most appropriate RMO should be considered and discussed prior to proposing substances for inclusion to the Candidate List; while the decision to include substances in Annex XIV is taken by the Commission via the regulatory procedure with scrutiny under Article 133(4). While we acknowledge the desire for regulatory consistency, we also recognise the challenges both in defining the scope of such consistency and in achieving such consistency in general, and in

			priorisation the Finnish CA consider it necessary having assessed as far as possible the most efficient and practical risk management measures before final inclusion of a substance in the Annex XIV. Ideally, issues concerning risk management options should be thoroughly examined and solved prior to proposing substances to the candidate list or at least, in the regulatory procedure referred to in Article 133.4.	particular during the recommendation step of the authorisation process. Consistency may help (i) in increasing efficiency of the regulatory actions, in particular where the differences in the actions could result in an unwanted transfer to (similar) substances without reducing the risks, (ii) to enhance predictability of the authorities actions and (iii) to support achieving a level playing field. The consistency of regulatory actions can however be viewed from multiple angles and achieving consistency with one aspect may result in reduced consistency with another aspect. When seeking consistency there is a need to ensure that there is no undue delay in proceeding with regulatory actions and that the burden of proof is not reverted to authorities to make an upfront assessment of the substance and all its possible alternatives / similar substances. **Availability of suitable alternatives** The obligation to apply for authorisation is an incentive to search for and develop suitable alternatives. While in the short term there appear not to be alternatives, the authorisation title of REACH gives a long term incentive to find them and deploy them when these alternatives are technically and economically feasible. The authorisation process foresees that the availability of suitable alternatives for a use of an SVHC are addressed at the application phase of the authorisation process because it is this phase where the respective assessment can be done in an effective matter: based on structured input of information by the applicant; the foreseen dedicated public consultation for scrutinising this information; and the involvement of Committees having the respective expertise and mandate. Information on (lack of) availability of alternatives as well as the research and development efforts done are taken into account. Furthermore, the socio-economic benefits of the continued use(s) are

				an important basis for the Socio-economic Analysis Committee when it gives its opinion on, for instance, the length of the review period. Naturally the information of the availability (or non-availability) of alternatives is an important element when the final decision by the Commission is taken on whether to grant the authorisation. In addition to the incentive to search for alternatives, documenting this search and having it reviewed, the authorisation requirement also provides an additional level of scrutiny on the control of risk, including a possibility to impose further conditions, where needed. **Imported articles** It is noted that the prioritisation of DMF does not relate to its possible presence or lack of presence in (imported) articles. 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.
2425	2013/09/23 15:08	VOWALON Beschichtung GmbH , Company, Germany		-
2423	2013/09/23 15:01	Company, Czech Republic	The use of DMF for the production of intermediates for the synthesis of APIs (pharmaceutical industry) is performed within enclosed equipment in accordance with Good Manufacturing Practices (GMP), with respect of the intermediates used in the fine chemicals, in accordance with the REACH Regulation.	Thank you for your comment. If you decide to apply for authorisation of your uses of the substance, information brought forward in your comment can be included in the 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.
2420	2013/09/23 14:50	Allgemeine Unfallversicherungsanstalt, National Authority, Austria	DMF is a well known aprotic solvent that shall only be used in a well controlled industrial setting and in a laboratory by well trained professionals. Therefor we support that DMF will be included in Annex XIV. Due to Registration data the substance is used at industrial sites in closed systems with onlyallow very low levels of exposure (PROC 1, PROC 2, PROC 3) but also in systems where potential for significant exposure arises (e.g. PROC 4, PROC 5, PROC 8a). Potential authorisation will have to respect this.	Thank you for providing your opinion.
2418	2013/09/23 14:26	Hungarian Pharmaceutical Manufacturers Association, Industry or trade association, Hungary	DMF (N,N-Dimethylformamide (CAS No. 68-12-2) is used by the Member Companies of The Hungarian Pharmaceutical Manufacturers Association for the production of APIs used in the following important, and widely concerned therapeutic areas: cholesterol lowering drugs, psychiatric and neurological drugs, gynecological preparations, glaucoma drugs, treatment of hypertension, antiemeticums, serotonine 5-HT receptor antagonist drugs. Our annual consumption of DMF is around 100 tons/year. Many new drugs and a large number of relating intermediates are under development at Member Companies of The Hungarian Pharmaceutical Manufacturers Association where the solvent is used in any phase of the manufacturing process and this forecasted, but not awaited procedure jeopardizes continuing the manufacture in Europe. We would like to stress two major approach in our comment: • The substance is less harmful to the health and environment as its possible substitutes, and the substitution arises various further questions. • The pharmaceutical use with the best available technology (BAT), regarding the IPPC (newly: IED) directive of EU ensures that emissions are under controll and remain below the existing strictest exposure limit. Because of the above reasons we kindly ask ECHA to accept uses below the existing IOEL to get exemption from the authorization obligation. We stress that considerable energy is invested into selecting the safest and environmentally the most	Thank you for your comment. **Art 58(2) exemption response, Cost of substitution** Please see response to comment 2456, 2455. **Exemption: more harmful alternatives** Please note also that 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 companies 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 they currently use and of any potential alternative substance or technology. **ECHA's guidance on registration allows, under certain conditions, the use of an IOEL as a DNEL.** Please note that the prioritisation approach which was agreed and applied here to prioritise and

			humane manufacturing route already in the initial phase of the life cycle of the new drugs. Once the manufacturing route is selected for the new drug it becomes very difficult, time consuming and costly to change it and the change has to be justified due to the regulatory requirements in place to prove the efficacy and safety of the given route and the . One has to prove that the change (in our case the change of solvent) would not cause quality deterioration to the drug. As a dipolar aprotic solvent, DMF is widely used in the synthesis of active pharmaceutical ingredients (APIs) and associated intermediates. Reasons for the widespread use of DMF include: • DMF 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. • DMF additionally offers sufficient solubility of many inorganic reagents (e.g. acids & bases), helps to increase to efficiency rate of synthesis, and 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 DMF are essential for these reactions, since they prevent unreacted materials from being carried forward in the process stream, minimize the formation of side products, waste and produce intermediates and API of the highest quality. • The use of DMF can be essential (due to its 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 (153oC) – 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	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. As stated in the background document ECHA has assessed that there are industrial uses of DMF which have a potential for significant exposure. Whether or not exposure levels exceed valid DNELs is not part of the assessment. 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. Please consider 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.

			operationally feasible in typical pharmaceutical reactors, and inherently of greater operational hazard). • Low vapor pressure, much lower than water – which causes that DMF as many other dipolar aprotic solvents does not evaporate easily and such does not pollute air and atmosphere to a high concentration, finally in high volume contrary to many other solvents. As a consequence it is a much less harmful liquid for the environment as a whole. • There are other dipolar aprotic solvents with similar physical properties that could potentially be used in place of DMF in some manufacturing syntheses. However, a comparison of the three most widely used polar aprotic solvents DMF, DMAc and NMP using the 'Substitute Substance Check' (TRGS 600) tool indicates that the hazardous properties of these three substances are similar. These alternatives are all reprotoxins, carrying the H360D hazard statement and hence are at some stage in the SVHC authorisation processs rendering them unsuitable as long term alternative. The replacement of DMF with solvents having lower polarity could lead to incomplete reactions and side products that impact the safety and quality of the active ingredient for pharmaceuticals and veterinary medicines. This might increase waste streams. While the usage of DMF is controlled at the workplaces of pharmaceutical industry, recognising that Council Directive 98/24/EC (Protection of Workers from Chemical Agents) and amending Directive 2009/161/EC sets an indicative occupational exposure limit value (IOELV) for DMF, and thus, sets minimum requirements for the protection of workers in the chemical industry, it is our position that the use of DMF as solvent in the pharmaceutical manufacturing, should be exempted from the authorisation process, in line with Regulation (EC) No 1907/2006 of the European Parliament and of the Council, Article 58. (2). SCOEL values are implemented in the EU via a directive setting IOEL (Indicative OEL) or BOEL (binding OEL) and a date for implementation into national law. In case of a national limit value deviates from IOEL, the member state has not only has to notify the Commission, but give scientific justification as well. However, the Commission can initiate regulatory responses to such as regulations	

			which are binding to all member states. Nineteen member states have implemented the following IOEL for DMF: 8 hour TWA: 5 ppm (15 mg/m³) STEL (15 min): 10 ppm (30 mg/m³) The remaining member states that do not comply with the IOEL have not up-dated their OEL for seven or more years. This means that these member states established their national OEL before 2009 in which the IOEL was settled. The IOEL for DMF has been used to establish a DNEL: Worker Long-term exposure – systemic effects, dermal: 3.31 mg/kg Worker Long-term exposure – systemic effects, inhalation: 15 mg/m3 "A registrant is allowed to use an IOEL as a DNEL for the same exposure route and duration, unless new scientific information that he has obtained in fulfilling his obligations under REACH does not support the use of the IOEL for this purpose." [Chapter R.8: Characterization of dose [concentration]-response for human health p. 137]. According to the ECHA guidance, which are the own rules ECHA has given itself and consequently has to accept, IOEL values are valid DNELs to be accepted for occupational uses. If the CMR properties were considered when deriving the IOEL there is no scientific reason for ECHA not to accept the IOEL unless new experimentally data has been generated. The fact that a substance is recommended for authorisation is not new scientific information with respect to health effect. ECHA guidance should not arbitrary used or ignored by ECHA if it suits ECHA in certain cases. The relevant legislations are attached to the comment.	
2415	2013/09/23 14:02	Individual, Italy	From Annex XV results that DMS is largely used as a polar aprotic solvent in the production of intermediates. DMF has a harmonised classification that evidences that it is dangerous for the human health but not for the environment. Annex XV also mentions that DMF is included in the third list of indicative occupational exposure limit values (IOEL) set up by Commission Directive 2009/161/EU. The IOEL values for DMF are 15 mg/m3 (TLV-TWA) and 30 mg/m3 (TLV-STEL). Endura believes that these values should be used as a minimum requirement for the	Thank you for your comment. **Art 58(2) exemption response** Please see response to comment 2456. **Exemption (no suitable alternative)** Please refer to response to comment 2456. **Other RMO**

			protection of human health during the use of DMF. Moreover, the REACH regulation establishes that a substance is classified as intermediate if it is only used in processes where it is transformed into another substance under strictly controlled conditions (see articles 3(15a), 17 and 18 of REACH). This means that companies using DMF in the synthesis of intermediates will apply the strictly controlled conditions described in "Guidance on intermediates – Version 2 December 2010" edited by ECHA (otherwise the company would have the obligation to submit a full REACH registration dossier for all intermediates synthesized). Finally, Article 58(2) of REACH establishes that certain uses or categories of uses may be exempted from the authorisation requirement if the risk connected to these uses is properly controlled. In Endura's opinion, and in agreement with what is reported above, the DMF used as a solvent for the production of intermediates complies with the case described in Article 58(2) of REACH and, for this reason, it should be exempted from the authorization requirement. Another important aspects regards the fact that, as reported on page 8 of Annex XV, the largest user of DMF in the world is China. We believe that if DMF will be banned from the EU market the problem of the products (not only articles but also mixtures and substances that can contain DMF as impurity) contaminated with DMF will not be resolved. In fact, the importation of products, that require the use of DMF during the manufacturing process, from China will likely increase. This is difficult to control and could consequently results in the EU in an increase of products contaminated by DMF. It could furthermore encourage European companies to outsource part of their activities to non-EU countries. Finally, it results from Endura's investigations that alternative solvents, polar and aprotic at the same time and equivalent to DMF in terms of efficacy and efficiency but with a lower hazard profile, do not exist (e.g. Dimethylacetamide EC: 204-826-4 and Hexamethylphosphoramide EC: 211-653-8, are equivalent in terms of efficacy/efficiency but are not less hazardous than DMF). By virtue of the above considerations, we conclude that	Please see response to comment 2427 in this section. **Authorisation perceived as a ban of DMF, favouring relocation outside EU - increased risk for import of mixtures and/or articles containing high levels of DMF as their control are difficult** Please consider that 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. Furthermore, please note that authorisation requirement applies to mixtures (at or above the concentration limit for the substance) regardless of whether they are produced in the EU or they are imported. 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.

			the Restriction process rather than the Authorization process, could be the best solution to control the risk deriving from the use of DMF as solvent for the manufacturing of intermediates and in the production the articles. Finally, in the case of articles production we also think that the Restriction would allow to improve the control on the finished articles coming from non-EU countries, thus reducing the percentage of products contaminated with DMF on the EU territory.	
2414	2013/09/23 13:38	Company, Germany	Abbott is a global healthcare company devoted to improving life through the development of products and technologies that span the breadth of healthcare. With a portfolio of leading, science-based offerings in diagnostics, medical devices, nutritionals and branded generic pharmaceuticals, Abbott serves people in more than 150 countries and employs approximately 70,000 people. In the EU, Abbott has major manufacturing facilities in Ireland, United Kingdom, Germany and Spain. Diagnostics: Abbott is a global leader in diagnostics (medical devices and in vitro medical devices (IVDs)) offering a broad range of innovative instrument systems and tests for hospitals, reference labs, blood banks, physician offices and clinics. Our products provide customers automation, convenience and flexibility, all of which lead to cost effective care. Key areas of focus include core laboratory diagnostics, immunoassay and clinical chemistry systems, hematology, molecular diagnostics and point of care diagnostics. Vascular Products: Abbott Vascular is the world's leader in drug eluting stents. Abbott Vascular has an industry-leading pipeline and a comprehensive portfolio of market-leading products for cardiac and vascular care, including products for coronary artery disease, vessel closure, endovascular disease and structural heart disease. Vision care: Abbott Medical Optics is focused on delivering life-improving vision technologies to people of all ages, offering a comprehensive portfolio of cataract, refractive and eye care products. Products in the cataract line include monofocal and multifocal intraocular lenses, phacoemulsification systems, viscoelastics, and related products used in ocular surgery. Products in the refractive line include wavefront diagnostic devices,	Thank you for your comment. **Consistent approach with similar solvents** Please refer to response to comment 2427 in this section. **Production outside EU to ensure security of the supply** Please refer to response to comment 2455 in this section. **Socio-economic impacts of substitution and no safe alternatives** Please refer to response to comment 2455 in this section.

			femtosecond lasers and associated patient interface devices; excimer laser vision correction systems and treatment cards. Products in the eye care line include disinfecting solutions, enzymatic cleaners, lens rewetting drops and artificial tears. Diabetes: Abbott Diabetes Care is a leader in developing, manufacturing and marketing glucose monitoring systems designed to help people better manage their diabetes. N, N-dimethylformamide (DMF) is used in the production of in vitro Diagnostic Medical Device (IVDs) and medical devices that are produced and marketed in the EU and regulated under the In Vitro Diagnostic Medical Device Directive 98/79/EC and Medical Device Directive 93/42/EEC, and. One of the main objectives of these directives is the maintenance and improvement of the level of health protection attained in the Member States, as well as to allow the free movement of such devices within the EU. Subjecting the use of DMF in manufacture of ingredients used in IVDs to authorisation and forcing their eventual substitution would almost certainly contravene this objective. The use of DMF in the manufacture of these devices as reagents along with the control and calibration of these types of devices is crucial to the continuing production of these devices within the EU. Current manufacturing for many of these lifesaving products occurs in the European Union and supplies the global healthcare market. Thus, the potential authorization requirements for DMF as a process solvent in the manufacture of IVDs, impacts not only the EU healthcare market but the global IVD healthcare market. Substitution of DMF will be a complex, time consuming process subject to approval by many regulatory agencies worldwide. Throughout this substitution, our focus will be to ensure these lifesaving products are available globally without interruption to the public and medical community. Although every effort will be made to achieve appropriate substitution, it is possible that the product critical attributes could be affected (including specificity and sensitivity), thereby affecting the quality of the test results and therefore medical care worldwide. As a result, some manufacturing may need to be deferred to other	

			locations outside the EU to ensure global supply can be uninterrupted. Dimethylformamide is a member of a group of extremely useful and widely used polar aprotic solvents. Within the in-vitro (IVD) medical device industry, DMF and similar solvents (DMAC, NMP) are used as process solvents in the production of IVDs and associated reagents and as standard analytics in laboratory research and development. In some cases, the DMF does not remain as a constituent in the final IVD. While there are other polar aprotic solvents with similar physical and chemical properties that could potentially be used in place of DMF, these alternative solvents also carry essentially the same health hazard as DMF. DMAC and NMP are currently progressing through the committee stages of two separate risk management processes: Authorisation and Restriction. The final decision to include other aprotic solvents (DMAC, EDC) onto Annex XIV is to be taken later this year by EU Committee under ECHAs 4th recommendation. Concurrently, a restriction proposal for NMP has been published for public consultation and is currently being considered by another ECHA committee. Since an iOELV has been set by SCOEL for DMF which has been adopted by several member states into National Legislation, control of occupational exposure below a 'specified level' can already be demonstrated. There is an obvious regulatory inconsistency in so far as similar substances are being treated under different risk management measures for the same uses that could act to undermine the REACH processes that were designed to protect human health and the environment from the harmful effects of chemicals. It would therefore be appropriate that the inclusion of DMF onto Annex XIV be postponed until the outcomes of both Committee procedures are known and a consistent and appropriate risk management approach to the aprotic solvents is agreed. It is anticipated that the use of DMF in IVDs will not be subject to Authorisation in accordance with article 60(2). However, other uses such as a process reagent in the manufacturing of IVDs including use as a solvent in the synthesis of ingredients of reagents which are used in IVDs may not be explicitly exempted from the	

			requirements of authorisation by this article. Authorization of DMF would have a critical impact on the IVD industry as outlined in the section on transitional arrangements. In summary, Abbott strongly opposes the inclusion of DMF onto Annex XIV at this time on the basis that there appears to be a large degree of uncertainty around the application of a consistent REACH regulatory measure for the group of aprotic solvents. Use of the substance in the manufacture of IVDs and medical devices is already regulated under the medical devices directives and occupational exposures are controlled in accordance with the Chemical Agents Directive.	
2411	2013/09/23 13:31	Company, Finland		-
2383	2013/09/23 11:13	CEPSA S.A.U., Company, Spain	Cepsa does not agree with conclusion stated in draft priorisation report, since authorisation is not the most suitable risk management option to handle dmf exposure. Most of uses take place at industrial sites under highly contained conditions, whithout subsequent life stages, other than waste disposal according european legislation. Worker exposure are minimized through Occupational Exposure Limit (IOEL: 8h-TWA 15 mg/m³; 15 min STEL 30 mg/m³) and other regulations (Directive 98/24/EC ("Chemical Agents Directive"), Directive 92/85/EEC (concerning pregnant workers)). Moreover, since dmf falls under VOC definition, Directive 2010/75/EU (on industrial emissions) shall be observed. Its substitution would impact negatively in affected sectors, since there is not a suitable and safer alternative. Dmf is part of aprotic solvents family, N,N-dimethylacetamide (DMAC), N-methylpyrrolidone (NMP) and N-ethylpyrrolidone (NEP) are probable substitutes but with equivalent concern. A substitution would impact to authorisation of products (in medicaments and veterinary) and would carry high expenses in new revision. Relating priorisation score, Cepsa does not agree with given value. There are less use sites that mentioned since use in laboratories are exempted, and use cannot be considered wide dispersive/uncontrolled, since takes place at industrial places. Thus Cepsa proposes revision	Thank you for your comment. **Other RMO** Please refer to response to comment 2427 in this section. **Risk controlled by existing regulation, No safer alternative, High costs of substitution process** Please refer to response to comment 2456. **WDU score** Please refer to response to comment 2488.

			of verbal-argumentative approach to reduce its prioritisation score.	
2381	2013/09/23 11:06	Company, Ireland		-
2374	2013/09/23 10:01	Company, Sweden	The need for REACH authorization upon use of N,N-dimethylformamide (DMF),EC number 200-679-5, as a process solvent in the manufacture of Active Pharmaceutical Ingredients (APIs) by the Pharma Industry , is of much concern. There are currently no known technically equivalent substitutes for the use of DMF as process solvent and besides other polar aprotic solvents, DMAc, NMP and NEP which could be considered, no other less polar solvent shows the same powerful solvating properties as DMF. The possible effects of an authorization process for polar aprotic solvents, such as DMF, would cause an uncertainty in the Pharmaceutical industry since an REACH authorization is not automatically granted and also limited for a certain timespan. Furthermore, the impact of exchanging DMF and other polar aprotic solvents in current manufacturing processes for Active Pharmaceutical Ingredients (APIs) and associated intermediates would require time consuming research and product development, huge costs for the Pharmaceutical industry and increased drug evaluation and animal testing. This would in turn most likely make the Pharmaceutical Industry in the EU turn to manufacturing in non-EU countries to be able to proceed with research & development and manufacturing of Active Pharmaceutical Ingredients (APIs), as the authorization requirement is only applicable on the manufacturing process: the final product is exempt Furthermore, contract research organizations (CRO) and contract manufacturing organizations (CMO) within the EU would also see potential new drugs being developed and produced by their competitors located outside the -EU . These factors should be considered before DMF or other aprotic solvents are recommended for authorization as other risk management options may be more appropriate to address concerns associated with potential exposures to these substances. In the least, as explained further below, their use as a solvent or	Thank you for your comment. **Other RMO** Please refer to response to comment 2427 in this section. **Delocalisation outside EU** Please refer to response to comment 2415 in this section. **Competitive disadvantage** Please refer to response to comment 2488 in this section. **Exemption, No safer alternatives, Increased animal testing, High cost of substitution** Please also refer to response to comments 2455 and 2456.

			processing aid to manufacture medicinal products should be exempt from authorization.	
2368	2013/09/23 04:32	Company, United Kingdom	The 'background document for N, N-Dimethylformamide [DMF]' recommending its inclusion in Annex XIV has not adequately addressed the initial comments received from stakeholders of DMF on the Annex XV dossier. The recommendation concludes in its justification for prioritisation "The substance is used in very high volumes in the scope of authorisation. The substance is expected to be used at high number of sites. For some operations significant potential for workers exposure cannot be excluded", without providing a definition for the criteria used to reach conclusions on high volume, high number of sites, or operations with significant potential for exposure to workers. In the words of the Member State United Kingdom (reference form General comments on SVHC proposal – 17 2012/10/16) "It would be useful to clarify whether this substance is creating a real risk before it is considered in any prioritisation for inclusion in Annex XIV. It would also be useful to assess whether other technologies or management practices could be effective to prevent worker exposures in operations of concern in lieu of imposing regulations that could disrupt the supply of life-saving medicines. DMF is used as a process chemical in the manufacture and dispensing of chemical dyes, fine chemicals and chemical products. The products produced using DMF are in turn used in medical research and development and DO NOT contain DMF. The use categories for these applications are subject to the existing Community legislation, imposing requirements for safe use of the DMF and proper control of any risks, under the United Kingdom's [UK] Control of Substances Hazardous to Health Regulation [COSHH] [2002], as amended http://www.hse.gov.uk/coshh/detail/reach.htm. We request consideration should be taken for the existing legislation imposing risk management measures protecting human health and the environment COHHS legislation, in addition to the UK Health and Safety at Work Act 1974, and European Communities Act 197 impose requirements relating to the protection of human health or the environment for the use of DMF, under	Thank you for your comment. **Exemption art 58(2)** Please see response to comment 2456. **Prioritisation should have assessed risks** 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. **Definition of the criteria used for prioritisation not clear** 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/docu+E2ments/10162/17232/axiv_priority_setting_gen_approach_20100701_en.pdf). The document provides a definition for the criteria used to reach conclusions on high volume, high number of sites, or operations with significant potential for exposure to workers. Further explanations and justification for the scoring of the 'wide-dispersive use' criterion is

			Article 58[2]. The application for Authorisation would demonstrate there are no technically equivalent alternatives to DMF for the specific use applications in medical research and development, and product and process oriented research and development [PPORD]. Therefore, it is requested that the categories of uses including medical research and development and PPORD be exempted from the Authorisation requirements. Please reference the position paper submission of EDMA, Comments on the draft recommendation of substances for inclusion in Annex XIV Substance name: Dimethyl Formamide [DMF] Consultation deadline 23 September 2013.	provided in the response to comment 2488. **Comment from stakeholders not taken into consideration** Note that for applying its prioritisation approach on DMF, ECHA assesses all the available information. In this context, information collected during the development of the Annex XV Dossier, from the Registration Dossiers incl. the CSRs and data submitted during the public consultations has been taken into account and summarised in the Background Document. Please also refer to response to comment 2455.
2365	2013/09/22 22:22	Company, Germany		Thank you for your comment. **Exemption art 58(2)** Please see response to comment 2456. In addition, according to Art. 56(4) REACH, substances used in plant protection products within the scope of the relevant EU legislations are exempted from authorisation. Regulation 1107/2009 concerning the placing of plant protection products on the market includes a risk assessment and authorisation procedure for active substances and products containing these substances, including the relevant transitional measures applicable to certain provisions of Directive 91/414/EC. Under this Regulation, DMF is not an approved substance. Therefore, the exemption in Article 56(4)(a) REACH cannot apply. It needs to be examined whether an exemption can be granted under Article 58(2) REACH. The plant protection product legislation does not appear to control risks to human health or the environment arising from the manufacturing stage of these products or, in particular, from the solvent use and disposal of DMF. Therefore, this legislation may not be regarded as a sufficient basis for exempting this use of DMF from authorisation in accordance with

				Article 58(2) of the REACH Regulation. **Exemption: not WDU, no safer alternative, cumbersome revalidation process, additional animal testing** Information on the low level of risk or exposure associated to a use or related to the availability and suitability of alternatives as well as to the complexity and the (economical) consequences of re-registration processes are important. Information regarding these topics should be provided as part of the application for authorisation. 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. Further information on the justification and scoring of the 'wide-dispersive use' criteria is provided in the response to comment 2488.
2356	2013/09/20 20:21	Company, France	We do not really understand why the DMF is priorised for inclusion in Appendix XIV since the background document indicates that : - the substance is mainly used by industrial in closed of semi-closed system - there is no safe alternative to DMF for this type of solvent and the interdiction of DMF would limit the number of chemical reaction used to produce active ingredients (eg : pharmaceuticals) - it is possible to minimize the exposure risk for employees using technical containment means (with individual protection in addition) The restriction way could have been another solution to avoid specific uncontrolled industrial applications.	Thank you for your comment. **Other RMO** Please see response to comment 2427. **Reasoning for prioritising DMF** With regards the reasoning for prioritising DMF, please consider 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/docu+E2ments/10162/17232/axiv_priority_setting_gen_approach_20100701_en.pdf). Consequently information on topics such as the availability and suitability of alternatives 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. Instead the prioritisation approach is intended 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. Further justification on the prioritisation is provided in the response to comment 2488.
2354	2013/09/20 19:46	Company, France	In our activity, production of medical device, the use of DMF as solvent is a key point at the beginning of the process to obtain our products. No other way are available than the use of solvent. Our products have a direct impact on the safety of the patients, and can not be replace with the same level of efficiency and comfort for our patients. As mentioned in the Draft background document for N,NDimethylformamide (24 June 2013), replacement of DMF is not possible with safe solvent. And for one specific process, there is no alternative. As DMF is only used in closed processes and s the level of protection for workers and environment is already high, we consider that to include DMF in Annex XIV is not necessary. To include the substance in Annex XVII is a most accurate solution. To include DMF in Annex XIV, with, for consequences, the removal of DMF, might induce for our plant the stop of production due to - the need to chose a solvent with the same level of risk for safety and environment, and the possibility that the solvent will also be included in Annex XIV, - the cost of investments in process development and in equipment linked to the change of solvent, - the cost of validation and registration of the products The consequences will be the close of the plant and the sales and marketing services linked to the products.	Thank you for your comment. **No alternative and other RMO** Please refer to response to comment 2427. **DMF use pattern in specific industrial sectors/companies** Please refer to response to comment 2456. **Authorisation perceived as a ban** Please refer to response to comment 2415. **Substitution cost, socioeconomic considerations** Please see response to comment 2455.
2353	2013/09/20	Company, Belgium		Thank you for your comment.

	19:42			**Exemption art 58(2) and principle of proportionality** Please see response to comment 2456 and 2488. **Intermediate status** In addition, note that the intermediate status of a substance has to be carefully assessed. According to Appendix 4 of the "Guidance on intermediates" (http://echa.europa.eu/documents/10162/13632/intermediates_en.pdf) from December 2010, "An isolated intermediate (i.e. a substance "used […] in order to be transformed into another substance"), is used in the manufacturing of another substance where it is *itself* transformed into that other substance. […] Whenever a substance (A) used in a chemical processing is not used in the manufacturing of another substance (B) in order to be itself transformed into that other substance (B), it is necessarily used in order to achieve another function than transformation. As soon as the main aim of the chemical process is not to transform a substance (A) into another substance (B), or when substance (A) is not used for this main aim but to achieve another function (e.g. solvent), substance (A) used for this activity should not be regarded as an intermediate under REACH." If substance (A) is transformed into products of degradation which are discharged in air then further incinerated (= disposed as waste), products of degradation are not isolated, neither used nor registered. Waste is not a substance under REACH therefore in these cases conditions of art 3-15 (manufacturing of another substance) are not met. One obligation arising from inclusion of a substance in Annex XIV is the responsibility of actors to assess whether their uses of the substance are in the scope of authorisation (e.g. whether the use fulfils the definition of an intermediate as set out in Art. 3(15) of REACH) and to keep all relevant

				documentation supporting their respective conclusion. This information may be requested by any competent authority of the Member State in which he is established or by the Agency. Non-compliance with the requirements of REACH may result in enforcement actions by the competent authority of the Member State in which the actor is established.
2347	2013/09/20 18:27	Company, Ireland	Use in the production of active pharmaceutical ingredients (APIs) Dimethylformamide (DMF) is a frequently used important solvent for the manufacture of APIs. DMF is one of a class of polar aprotic solvents which are essential from a chemical synthesis perspective. Other solvents in this class e.g. N, N-dimethylacetamide (DMAc), 1-methyl-2-pyrrolidone (NMP), N-methylacetamide have already been included in the Candidate List of Substances of Very High Concern for Authorisation. The physical properties of these solvents make them an essential choice from a chemistry perspective in the synthesis of Active Pharmaceutical Ingredients (APIs), including peptides used in the treatment of rare, debilitating and life threatening diseases. DMF offers sufficient solubility of many inorganic reagents (e.g. acids & bases) that facilitates chemical reactions that would not be possible in many other organic solvents. In the manufacture of peptide APIs, it is a key solvent which ensures solubility of all reagents and protected amino acid building blocks, and facilitates amide bond formation. DMF also facilitates solid phase peptide synthesis by maintaining swelling of the resins used while also allowing reactions to proceed to completion. The manufacture of Active Pharmaceutical Ingredients (APIs) and associated intermediates are performed in enclosed reactor trains in accordance with Good Manufacturing Practices and in-line with best EHS and Engineering practice. DMF is dispensed into reactor vessels via transfer systems designed to minimise environmental release, by trained personnel using appropriate protective equipment. The activity is fully risk-assessed, and is supported by industrial hygiene	Thank you for your comment. **Exemption under Art 58(2)** Please see response to comment 2456. **No alternative, socio-economic benefits of the use, (negative) impacts of ceasing use, low risks** Please refer to response to comment 2455.

			monitoring, medical monitoring of personnel working in these areas, and enforced by audit. The residual amount of DMF allowed in APIs is limited according to the ICH Q3C guideline (Guideline for Residual Solvents). In practice all DMF used during API manufacture is present in the waste streams that are then disposed of in accordance with local and EU environmental regulations, and according to Integrated Pollution Prevention Control (IPPC) licence which is issued and audited by the national Environmental Protection Agency (EPA). Thus, the risks of environmental exposure of DMF in the pharmaceutical manufacturing environment are minimized by equipment design and operational controls; disposal and record-keeping procedures exist within the oversight of the quality and/or EHS systems. There are other polar aprotic solvents with similar physical properties that could potentially be used in place of DMF in some API manufacturing syntheses. The most common 'direct' alternative is DMAc (N,N-dimethylacetamide), however this has already been included in the Candidate List of Substances of Very High Concern for Authorisation . Others include formamide, N-methylformamide, 1-methyl-2-pyrollidone (NMP) and N-methylacetamide. However, these alternatives also carry similar or worse health hazards as DMF and would require re-submission of multiple regulatory dossiers for use in API manufacture, resulting in potential drug shortages while approvals are being granted. The use of DMF is specifically described in regulatory dossiers of APIs. There is no single alternative to DMF currently available which replaces the many uses and properties that DMF possesses; replacement of DMF cannot be done without process redesign, redevelopment and validation which are not economically viable and which take a very long time to complete; moreover further additional toxicological testing of APIs may be required as a result of the process change. Replacement of DMF in API manufacturing processes cannot be done without approval of all the relevant Pharmaceutical Authorities of every country where the medicine has been registered. It is our contention that not exempting DMF usage in the development and manufacture of APIs from authorisation will result in shortages of medicines	

			for life threatening and/or debilitating diseases such as cancer, acromegaly, diabetes, and osteoporosis. We believe it would therefore be appropriate for DMF to be exempted from authorisation for its use in the development and manufacture of active pharmaceutical ingredients as defined in Art. 1(2) of the Directive 2001/83/EC relating to medicinal products for human use. Furthermore, we contend that as the risk associated with the use of DMF in the development and manufacture of APIs is properly controlled from both human health and environmental perspectives, it should therefore be exempted from authorisation, in accordance with REACh article 58(2). Relevant EC Regulations The use of DMF in the manufacture of active pharmaceutical ingredients 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) ICH Q3C guidance on residual solvents (EMA/CHMP/ICH/82260/2006) contains a specific concentration limit for DMF. Occupational exposure is controlled through compliance with the Chemical Agents Directive (98/24/EC) on the protection of the health and safety of workers from the risks related to chemical agents at work. Commission Directive 2009/161/EU in implementing Council Directive 98/24/EC and amending Commission Directive 2000/39/EC sets an indicative occupational exposure limit values (IOELVs) for DMF for the protection of workers from chemical risks. These levels are then used by Member States to establish their own national limits. As the following safe limits have been set within EU law; 8 hour TWA: 5 ppm (15 mg/m³), STEL (15 min): 10 ppm (30 mg/m³).	
2343	2013/09/20	Individual, Italy	The substance has specific uses for which there are not potential alternatives with a lower hazard profile.	Thank you for your comment.

	17:33		Commission Directive 2009/161/EU of 17 December 2009 established the IOEL for DMF to be 15 mg/m3 (TLV-TWA) and 30 mg/m3 (TLV-STEL). We think that the IOELS values should be considered as binding values, and therefore should be accepted as a minimum requirement relating to the protection of human health and the environment for the use of DMF. Accordingly, we believe that the best solution is to attribute binding efficacy to IOELS values (by a directly applicable European regulation, if necessary) and that the uses or categories of uses that comply with Commission Directive 2009/161/EU are exempted from the authorization requirement, as indicated in REACH, Art. 58(2). Moreover, on pag. 15 of the annex XV dossier, there is written that there is no indication of substitution of DMF for its main industrial uses, so we think that the way of Authorization is a disproportionate measure for this substance and not the most appropriate Risk Management Option (RMO) for save uses. Consequently, and only in case it won't be accepted the IOELS values as binding values, we believe that it would be better to address the DMF in the process of restriction; in this way, the uses for which there are no substitutes and can be documented as safe in industrial processes, will be preserved. Another consideration concerns the statement on pag. 8, in which there is the notice that the largest consumer of DMF in the world is China; we think that the eventually future band of DMF, derived from the process of authorization, will not resolve the problem of articles with DMF put on the European market by Chinese manufacturers. As a matter of fact, the process of restriction would allow a greater control on finished articles coming from outside Europe. In addition, on the economical side, it has to be considered that the impact on some industries would be very high. In particular, if the DMF will be inserted in annex XIV of REACH, several manufacturings will close and many downstream users (in particular for the production of articles) will have problems to continue their activities. My company G. Crespi Spa one of the most important factories of synthetic leather has already reduced its staff from 350 to 150 people	**Other RMO, availability of suitable alternative, Imported articles**Please see response to comment 2427. **Art 58(2) exemption response** Please see response to comment 2456. **Competitive disadvantage and proportionality of the authorisation process** Please see response to comment 2488.

2341	2013/09/20 17:24	C.O.I.M. S.p.A., Company, Italy	We agree with the position explained by Federchimica (Italian Chemical Association)	Thank you for your comment. **DMF use pattern in specific industrial sectors/companies** Please refer to response to comment 2456. Also refer to response to comment 2295 (Federchimica).
2340	2013/09/20 16:37	Sioen Fabrics, Company, Belgium		Thank you for your comment. **Exemption: Article 58(2)** Please see response to comment 2456. **Added value of authorisation process** 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 authorisation procedure aims to progressively replace Substances of Very High Concern (SVHC) by suitable alternatives as soon as technically and economically feasible. Until substitution is achieved authorisation aims to ensure the good functioning of the internal market while assuring that risks arising from SVHCs are properly controlled. 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 DMF is toxic to 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 all the uses of this substance is protected while the substance will be progressively replaced by suitable alternatives where economically and technically viable. **Other RMO, Imported articles** Please see response to comment 2427. **Competitive disadvantage** Please see response to comment 2488.
2338	2013/09/20 16:21	Company, Netherlands	We acknowledge that the substance meets the criteria specified in Article 57 for designation as SVHC, specifically toxicity to reproduction pursuant to paragraph (c). Firstly however, the criteria listed in Article 58 (3), to be normally applied for inclusion in Annex XIV, have not been demonstrated to be fulfilled by the Agreement and Support Documents for the identification of the substance as SVHC as published by ECHA. Secondly, we request exemption for use as an industrial extraction solvent under conditions of rigorous containment in a process of recirculation. These conditions are equivalent to those for which exemptions are already recognized in Articles 2 (8 b) and 56 (4 c & d), and therefore while the process for requesting an exemption for such use under the current REACH legislation is unclear, subjecting it to authorization while exempting those equivalent uses would be discriminatory and therefore disproportionate. In view of these two points we request that this substance should not be prioritized for inclusion in Annex XIV.	Thank you for your comment. **Exemption: conditions of use equivalent to uses exempted according to Art. 2(8) and 56.** Please see response to comment 2456. **WDU scoring** Further justification on how DMF fulfils the criteria listed in Article 58 (3) is provided in the response to comment 2488.
2337	2013/09/20 16:20	Company, Germany	DMF was getting high priority due to the scoring approach in the background document "Draft background document for N,N-Dimethylformamide (DMF)" from June 2013. The total score is calculated as the sum of inherent properties IP, Volume V and the wide dispersiveness of the uses WDU. Most of our volume goes into the laboratory, QC and	Thank you for your comment. **Prioritisation justification** Please refer to response to comment 2488. **Other RMO, availability of suitable alternative** Please see response to comment 2427.

			R&D segment. The customers of this segment use DMF adequate to scientific R&D in volume below one tonne per year and under controlled conditions. Only a small part of our tonnage goes (5%) goes to industrial customers. These industrial customers are working in the Pharmaceutical, Diagnostics and Biotechnology/IVD area. From our point of view most of the DMF is used in small volumes under controlled conditions by trained persons. A small part of our total volume goes to industrial customers. The number of sites using DMF in an industrial setting is relatively low. Most of our customers are using the substance in a laboratory setting equivalent to scientific R&D. The scoring of 3 for the WDU is therefore not understandable to us. DMF is a common solvent for chemical reactions in scientific R&D. DMF is used in routine analysis (scientific R&D), especially for gas chromatography (GC) and for UV/Vis spectroscopy because it is a good solvent for many substances, including polymers and inorganic compounds. DMF is also used for analysis of residual solvents according to Ph Eur 7.7 (chapter 2.4.24) for headspace gas chromatography. Additionally, the substance is classified as class 2 residual solvent (solvents that should be limited in pharmaceutical products because of their inherent toxicity, see ICH Q3C Guideline for residual solvents) in pharmaceutical synthesis. Following the REACH regulation (Articles 56(3) and 3(23)) in combination with ECHA comments we come to the conclusion that the use of DMF as analytical standard and for testing of residual solvents is exempted from authorisation (scientific R&D). DMF is one of a class of extremely useful aprotic solvents. The physical properties of these solvents make them an attractive choice from a chemistry perspective in the synthesis of active pharmaceutical ingredients (APIs), excipients, and associated intermediates. DMF 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. For this reasons also we and our customers use DMF in the synthesis of pharmaceutical substances for medicinal products.	**DMF use pattern in specific industrial sectors/companies** Please see response to comment 2456. **Uses as analytical standard** As regards the use of DMF for analytical purposes, this may fall under the exemption of the use of substances in scientific research and development from the authorisation requirement in accordance with Art. 56(3). We would suggest that you examine whether the mentioned use of your substance for analytical purposes can be regarded as SRD in accordance with the definition set out in Article 3(23). Article 3(23) defines SRD as "any scientific experimentation, analysis or chemical research carried out under controlled conditions in a volume less than 1 tonne per year". It is noted that • SRD activities can cover analysis for monitoring or quality controls purposes; • Therefore, in principle a substance may be exempt from authorisation if used, on its own or in a mixture, in analysis for monitoring and quality control purposes, for instance, in order to monitor the presence or concentration of that substance or other substances; • Nevertheless, this exemption only applies to the extent that the relevant operator uses that substance under controlled conditions and in a volume less than 1 tonne per year. • It appears that only substances used directly for research or analytical purpose, whether on their own, in mixture, or in conjunction with analytical equipments, can benefit from the SRD exemption. This excludes from the exemption any substances forming an integral part of an analytical device. If you conclude that your use for analytical purposes of DMF fulfil the above points, that use can benefit from the exemption of SRD from authorisation as set out in Article 56(3) and no authorisation would be required to continue the use

			There are other polar aprotic solvents with similar physical properties that could potentially be used in place of DMF in some API manufacturing syntheses. The most common 'direct' alternative is DMAc (N,N-dimethylacetamide). Others include formamide, N-methylformamide, N-methylacetamide and N-methyl-pyrrolidone (NMP). However, these alternatives also carry essentially the same health hazard as DMF and are also in the SVHC focus. Following the above mentioned facts regarding the importance of DMF as solvent in the pharmaceutical industry and the absence of alternative solvents not showing reprotoxic properties we apply DMF not to be set on the authorisation list Annex XIV but to initiate a restriction procedure to minimize any danger to human health and environment posed by uses of DMF that are not under control as in the pharmaceutical industry.	after the sunset date.
2324	2013/09/20 15:26	Company, Belgium		Thank you for your comment. **Exemption Art 58(2), No alternatives, Risk controlled** Please see response to comment 2455 and 2456. **Other RMO / Imported articles** Please see response to comment 2427. **WDU** Further justification on how DMF fulfils the criteria listed in Article 58 (3) is provided in the response to comment 2488. **Delocalisation** Please refer to response to comment 2415.
2319	2013/09/20 14:24	Sanofi-Aventis SpA, Company, Italy	Legal Entity X is part of the Sanofi Holding a member of the ChemLeg Pharmaceutical Companies network which wrote a collective comment to the public consultation on the incorporation of DMF into the REACh Annex XIV. This comment is attached hereafter and has also been addressed to ECHA by the European Federation of Pharmaceutical Industries and Association	Thank you for your comment. Please see response to comment 2456.
2318	2013/09/20	Sanofi Chimie, Company,	Legal Entity X is part of the Sanofi Holding a member of the ChemLeg Pharmaceutical Companies network which	Thank you for your comment.

	14:21	France	wrote a collective comment to the public consultation on the incorporation of DMF into the REACh Annex XIV. This comment is attached hereafter and has also been addressed to ECHA by the European Federation of Pharmaceutical Industries and Association	Please see response to comment 2456.
2316	2013/09/20 13:35	Company, Italy	DMF (N,N-Dimethylformamide (CAS No. 68-12-2) is used by our company for the production of APIs used in the following important, and widely concerned therapeutic areas. Many new drugs and a large number of relating intermediates are under development at our company where the solvent is used in any phase of the manufacturing process and this forecasted, but not awaited procedure jeopardizes continuing the manufacture in Europe. DMF has specific uses for which there are not potential alternatives with a lower hazard profile. Commission Directive 2009/161/EU of 17 December 2009 established the IOEL for DMF to be 15 mg/m3 (TLV-TWA) and 30 mg/m3 (TLV-STEL). We think that the IOELS values should be considered as binding values, and therefore should be accepted as a minimum requirement relating to the protection of human health and the environment for the use of DMF. Accordingly, we believe that the best solution is to attribute binding efficacy to IOELS values (by a directly applicable European regulation, if necessary) and that the uses or categories of uses that comply with Commission Directive 2009/161/EU are exempted from the authorization requirement, as indicated in REACH, Art. 58(2). Moreover, on pag. 15 of the annex XV dossier, there is written that there is no indication of substitution of DMF for its main industrial uses, so we think that the way of Authorization is a disproportionate measure for this substance and not the most appropriate Risk Management Option (RMO) for save uses. Consequently, and only in case it won't be accepted the IOELS values as binding values, we believe that it would be better to address the DMF in the process of restriction; in this way, the uses for which there are no substitutes and can be documented as safe in industrial processes, will be preserved. Another consideration concerns the statement on pag. 8,	Thank you for your comment. **Proportionality of the authorisation process** Please refer to response to comment 2488. **WDU scoring** Further justification on how DMF fulfils the criteria listed in Article 58 (3) is provided in the response to comment 2488. **Exemption Art 58(2) ,** Please see response to comment 2456. **Other RMO, no alternative, imported articles** Please refer to response to comment 2427.

			in which there is the notice that the largest consumer of DMF in the world is China; we think that the eventually future band of DMF, derived from the process of authorization, will not resolve the problem of articles with DMF put on the European market by Chinese manufacturers. As a matter of fact, the process of restriction would allow a greater control on finished articles coming from outside Europe. In addition, on the economical side, it has to be considered that the impact on some industries would be very high. • There are other dipolar aprotic solvents with similar physical properties that could potentially be used in place of DMF in some manufacturing syntheses. However, a comparison of the three most widely used polar aprotic solvents DMF, DMAc and NMP using the 'Substitute Substance Check' (TRGS 600) tool indicates that the hazardous properties of these three substances are similar. These alternatives are all reprotoxins, carrying the H360D hazard statement and hence are at some stage in the SVHC authorisation processs rendering them unsuitable as long term alternative. The replacement of DMF with solvents having lower polarity could lead to incomplete reactions and side products that impact the safety and quality of the active ingredient for pharmaceuticals and veterinary medicines. This might increase waste streams. On the scoring: We challenge the scoring that has justified this prioritisation: • DMF has scored 0 (lowest possible) in terms of its inherently hazardous properties. This appears corrects as DMF is not a PBT or vPvB substance. DMF qualifies to be considered for SVHC only on the basis of "hazard to the unborn child" (H360D). • DMF exposure routes has been scored as 3x3=9 (highest available score). Sites The data in our possession show that the number of sites is very limited compared to other chemicals. Differently from what is stated in ECHA's draft background document, DMF is not used throughout the EU at hundreds of use sites, since we believe the number of sites is much lower. Therefore the score equal to 3	

			doesn't appear rightful, in our opinion the score should be 1. Release In addition, a score equal to 0 (insignificant) would be more appropriate for "significant potential for worker exposure from uses within the scope of authorisation", on the basis that the uses of DMF are controlled, safe and not widespread (industrial only). DMF is used in closed units, under suction systems, stored in closed vessels, transported and used under strictly controlled conditions. Exposure of workers in is regulated (IOEL) and personnel handling DMF in industry is well educated. Furthermore we believe that the use of DMF is wide spread and not wide dispersive. Wide-dispersive uses are characterised by use(s) of a substance on its own, in a preparation or in an article at many places (sites) that may result in releases and exposure to a considerable part of the population (workers, consumers, general public) and/or the environment. This means that uses taking place at many places, which however do not result in significant releases of a substance, may be considered only as 'widespread' but not as 'wide-dispersive'. With regard to the DMF risk management measures are in place to control workplace exposure and emissions to the environment. Hence we can not agree that a score of 9 is given to "wide dispersive use". Consequently the overall score is 9 = IP + v + WDU= 0 + 9 + (1*0).	
2315	2013/09/20 13:32	Company, Germany	Please refer to the attached document (non-confidential and confidential part)	Thank you for your comment. **Exemption art 58(2)** Please see response to comments 2456 and 2365. Please note, that in addition to the Art 58(2) exemption responses provided above it is not clear that the uses for which exemption is requested (i.e. use of DMF as an industrial process solvent in industrial installations – e.g. in chemical synthesis and in the industrial manufacture of fibres and membranes) would in all cases be covered by Chapter V of the IED relating to special provisions for installations and activities using organic solvents.

				In addition, regarding the reference to the Waste Framework Directive (2008/98/EC), this aims at, inter alia, protecting the environment and human health by preventing or reducing the adverse impacts of the generation and management of waste (including hazardous waste). Wastes classified as hazardous are considered to display one or more of the properties listed in Annex III of the Directive - which includes CMR properties. Wastes classified as hazardous feature on the list established by Commission Decision 2000/532/EC. Wastes from industrial activities containing reprotoxic solvents – such as DMF – are listed as hazardous waste and need to be treated accordingly. The Waste Framework Directive in general contributes to environmental protection at the waste life cycle stage. Waste including reprotoxic solvents is specifically listed as hazardous waste and therefore there appears to be minimum requirements related to the waste stage of this use. However, as outlined in the responses to other comments, there does not appear to be sufficient protection of man via the environment at other life cycle stages of this specific use. **Competitive disadvantage , Authorisation requirement is disproportionate / of no added value** Please see response to comments 2488 and 2340.
2313	2013/09/20 13:08	Cefic Alkylamines Sector Group, Industry or trade association, Belgium	The Cefic Alkylamines Sector Group proposes considering the attached memorandum containing the legal analysis of the relevant EU legislation supporting an exemption of specific uses of the substance N,NDimethylformamide ("DMF",CAS# 68-12-2) under Article 58.2 of REACH, in the context of ECHA's fifth Recommendation for the inclusion of DMF in Annex XIV of REACH.	Thank you for your comment. **Exemption art 58(2)** Please see response to comments 2456, 2365, and 2315.
2312	2013/09/20 12:57	CHINOIN Private Co. Ltd., Company, Hungary	CHINOIN Private Co. Ltd. is part of the Sanofi Holding a member of the ChemLeg Pharmaceutical Companies network which wrote a collective comment to the public consultation on the incorporation of DMF into the REACh Annex XIV. This comment is attached hereafter and has	Thank you for your comment. Please see response to comment 2456.

			also been addressed to ECHA by the European Federation of Pharmaceutical Industries and Association. Introduction: The EU Pharmaceutical Industry's Chemical Legislative (ChemLeg) Working Group (each of them are members of EFPIA) requests that the use of DMF in the manufacturing of pharmaceutical 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 is exempted from REACH authorisation requirements. This exemption would also include all PPORD uses of DMF (up to 50ts/pa) in the production of medicinal and veterinary products. We believe this exemption should be granted because of the following key reasons: • Community Legislation relating to the Health, Safety and Environmental (HSE) control of DMF already exists in particular community legislation relating to Occupational Exposure Levels. ChemLeg members have DMF OEL monitoring data taken from various Active Pharmaceutical Ingredient (API) Manufacturing facilities across various Member States which can be shared with ECHA on request from ECHA; • Community Legislation covering substitution/replacement of DMF already exists under the Industrial Emissions Directive; • Use of DMF in pharmaceutical manufacturing is not wide dispersive • If technically possible at all (see reasoning below), DMF can only be substituted by other Aprotic Solvents with similar health hazards; • Substituting a solvent used in the manufacture of a commercially available Pharmaceutical Product may require additional human and animal testing (contrary to the principles of REACh); • Substituting a solvent used in the manufacture of a commercially available Pharmaceutical Product requires the current Marketing Authorisations (granted by the European Medicines Agency (EMA)) to be amended leading to excessive costs (3M – 12M EUR per product) and time delays; • REACH article 62(5)(b)(i) suggests that an	

			Annex XIV listed substance handled in a facility that is permitted by Directive 96/61/EC doesn't need to consider risks from Human Health or the Environment when submitting an application for an Authorisation Use of that Substance The amount of DMF manufactured and/or imported into the EU is, according to registration data, in the range of 10,000 – 100,000 t/y. No information on exports is provided. According to registration information complemented by information from industry consultations performed in 2011 and 2012 (Annex XV report, 2012; RCOM, 2012), 50% of the total volume (5,000-50,000 t/y) is used in the production of APIs or crop protection ingredients. The majority of the uses take place at industrial settings. There is no registered use for consumer products . Within the EU Pharma Industry, DMF is used at Bulk API Manufacturing Sites (there will be some use at small R&D facilities but these volumes of DMF are limited). According to the DG ENTR website, there are approx. 900 Bulk API Manufacturing sites across the EU-27 . In creating this consultation response, the Pharmaceutical Industry's Chemical Legislative Working Group accounted for 60 Bulk API Manufacturing sites of which 30 use DMF; extrapolating that data to the data on DG ENTRs website and we get a maximum of 450 individual Bulk Manufacturing Sites using DMF (or approx. 15 sites per Member State). DMF is used within the ChemLeg Group of companies under highly controlled conditions in batch production processes (which typically are run a few times per year/month at most pharmaceutical plants) and is therefore not considered as wide dispersive use nor is there a continuous potential for exposure. Benefits of Aprotic Solvents (such as DMF) in the Production of Medicinal Products DMF is an aprotic solvent used to manufacture Active Pharmaceutical Ingredients (APIs) for pharmaceutical products which treat potentially life threatening or debilitating conditions such as, Small Cell Lung Cancer, Cervical Cancer, Herpes Simplex virus, Varicella Zoster viruse, asthma, eczema and psoriasis. DMF is also used in Pharmaceutical lab R&D and as an analytical standard	

			for a number of medicinal products. The powerful solvating properties of Polar Aprotic Solvents (such as DMF) facilitate organic synthesis reactions which often, cannot be achieved in less polar solvents. Polar Aprotic Solvents offer general high solubility of many APIs and intermediates which often have poor solubility in less polar solvents. This also facilitates processes that require minimal solvent quantities, compared with the much larger volumes of other solvents that may be required. 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 DMF are essential for these reactions, since (a) they prevent unreacted materials from being carried forward in the process stream and (b) they minimise the formation of side products, thereby producing intermediates and APIs of the highest quality. There are other Polar Aprotic Solvents with similar physical or chemical properties (albeit of lower polarity) that could potentially be used in place of DMF in some API manufacturing syntheses. The most common 'direct' alternative may be DMAC. Others include formamide, N-methylformamide, NMP, NEP and N-methylacetamide. However, these alternatives carry essentially the same health hazard as DMF. Some of these solvents are already on the REACh Candidate List or have been proposed to Annex XIV or Restriction. In addition, these solvents may have different reactivity and so the replacement of DMF with such solvents could lead to incomplete reactions and side products that impact the safety, quality and yield of the API. Moreover, this may result in additional animal and human testing and waste streams. In other cases, the properties of DMF are so unique in effecting a desired reaction reactivity, selectivity, solubility, or purification that no comparable performance with any other solvent is known or the alternative solvents pose a greater environmental, occupational health, or other concern. Scoping work to identify alternatives to DMF in the manufacture of pharmaceutical products within the EU has been undertaken in the past with very limited success. Significant development work would be required to identify and validate viable alternatives involving	

			major changes to the manufacturing processes and the Marketing Authorisation (see below). Given the complexity of global supply chains, the ability of the pharmaceutical industry to secure a continuous supply of medicines to the market could be at risk if DMF was not available for use. Description of the Use of DMF in the Production of Medicinal Products The manufacture of APIs and associated intermediates are performed in enclosed reactor trains in accordance with Good Manufacturing Practices (GMP), implemented BAT for the manufacturing. DMF (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). Residual amounts of DMF in the eventual pharmaceutical product are safety-limited by the ICH Q3C (Guideline for Residual Solvents). So in practice, virtually all the DMF used during manufacture would be present in the waste streams (other than that lost through fugitive emissions) which is primarily disposed of via incineration (some recycling of DMF will occur). Altogether, the risks of environmental exposure of DMF in the pharmaceutical manufacturing environment are minimized by the equipment design and operational controls.	
2311	2013/09/20 12:55	Lapicor nv, Company, Belgium	Our Company Lapicor nv (former site of Landen Pharmachem nv) produces API's and uses Dimethylformamide in the production of the API. This API has an existing application for Diarrea and is used mostly in South America. At the moment he API is also in a faze 3 testing for the use in influenza treatment. The production API is of course discribed in a drug master file. If the use of N,N-dimethylformamide is going to be restricted it will possibly create problems in the production of the API. The dimethylfomamide is use specifically here because it nearly the only solvent in which the API can be dissolved. So the restriction of the DMF could create serious problems in the production of the API. Lapicor nv is a downstream user of this solvent. Ofcourse	Thank you for your comment. **Authorisation perceived as a ban** Please note that use of DMF will still be possible in the future, i.e. after the sunset date, provided authorisation is applied for and granted, e.g. in your case either to your company or to an actor up your supply chain for that use - provided that this use is in accordance with the conditions of the authorisation granted. 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

			we use the DMF in a closed system.	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 brought forward on the low potential for exposure (use in closed system) can be included in the application, in case 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.
2307	2013/09/20 12:13	SABIC Petrochemical s B.V., Industry or trade association, Netherlands	SABIC is of the opinion, that on the basis of its own uses of DMF as an extraction agent during the production of monomers (ethylene, propylene, butadiene), authorization of DMF is not necessary to achieve control of exposure. Moreover, even the authorization of DMF as such, for other uses, could well lead to a disruption of the market for DMF. This market disruption could make it impossible to acquire DMF in Europe at all, or at prices that would make economical production impossible. Technical changes of the production process, even if possible, would lead to very high investment costs. The final effect of cost increases or supply restrictions would be closure of the steam crackers and related polymer production of SABIC in Europe. Specific restrictions, such as proposed for NMP, would lead to a much more stable commercial situation that should enable a continued safe use and market supply of DMF.	Thank you for your comment. **Other RMO** Please see response to comment 2427. **Added value of the authorisation process** Please refer to response to comment 2340. **Uncertainty , Plant closure, Competitive disadvantage** Please see response to comments 2488 and 2415 in this section. **Risk controlled, No suitable alternatives** Please see response to comments 2455 in this section.
2299	2013/09/20 11:07	Company, Germany	In order to avoid the considerable economic disadvantages connected with a DMF treatment by way of authorization for producers in the "REACh" area (no real alternatives available in terms of performance, manufacturers outside of the "REACh" area can still use DMF, end products mostly contain residual DMF at a ppm level well below 50 ppm) and in view of the hazard potential of DMF the logical consequence must be that	Thank you for your comment. **Competitive disadvantage** Please see response to comments 2488 and 2415 in this section. **Other RMO, no suitable alternative** Please see response to comment 2427.

			risk management measures have to be defined for the different possible applications of DMF and every industrial application which is under normal circumstances evaluated as "safe" should be allowed – meaning that "DMF" should be treated under "REACh" in the process of "restriction" to industrial use. This treatment of course implies a safe and proper handling of DMF without any risk for those working with the substance or for the end users under foreseeable circumstances and normal conditions. These minimum requirements of indispensable and normal preconditions of a safe use of DMF relating to the protection of human health or the environment (in accordance with the EC dirctives like 2009/161/EC and 1999/13/EC) and thus properly controlling the risk in the case of a coating process are: a) Indispensable and normal preconditions of a safe use of DMF in the case of a usage in a production process are: 1. As far as possible closed production process ideally meaning no possibility for workers to have contact with DMF. If contact with DMF is inevitable, f.ex. when the DMF containing composition has to be pumped out of drums in order to be able to further process it in a coating station suction units are installed – generally suction units and ventilation are everywhere where there is exhaust air. The coating station itself and the following drying station are closed systems meaning that no exhaust air can escape – the coating station itself even is a double-closed system meaning that it is surrounded by a second cabin. At the end of the coating and drying processes the exhaust air is collected and treated in a special thermal exhaust cleaning system or a special incineration station with filters preventing any air pollution. The used filters as any other solid waste are collected in closed special containers with the necessary warning signs on them and disposed of in hazardous waste facilities. 2. Usage of breathing filters (type A), tightly closing protecting goggles and protecting butyl rubber gloves is obligatory for the workers. 3. Specialists in working security set up risk analyses for every production step, resulting in recognition of risk potentials and implementation of	**Risk controlled / low exposure** Please see also response to comment 2455.

			measures for safe use in every production step. The risk analyses are constantly and regularly carried out and updated every time the production steps are changed. 4. Legal Threshold Limit Values (TLVs) are constantly checked by experts in working security and the DMF concentration is constantly below these limit values. 5. Only well-trained and experienced personnel is employed in the production process. 6. There are no female workers involved in the production process. b) Indispensable and normal preconditions of a safe use of DMF in the case of a usage as a cleaning solution are: 1. Working as far as possible in a closed system (cabin with suction unit and a glove box from the outside), possible cleaning tanks connected with a suction unit, too. 2. Usage of breathing filters (type A), tightly closing protecting goggles and protecting butyl rubber gloves is obligatory for the workers. 3. Specialists in working security set up risk analyses for every production step, resulting in recognition of risk potentials and implementation of measures for safe use in every production step. The risk analyses are constantly and regularly carried out and have to be updated every time the production steps are changed. 4. Legal Threshold Limit Values (TLVs) are constantly checked by experts in working security and the DMF concentration is constantly below these limit values. 5. Only well-trained and experienced personnel is employed in the cleaning process. 6. There are no female workers involved in the cleaning process.	
2298	2013/09/20 11:06	Assogastecnici/Federchimica, Industry or trade association, Italy	Assogastecnici challenges the scoring (18/27) that led to the DMF prioritisation. • DMF has scored 0 (lowest possible) in terms of its inherently hazardous properties. It is opinion of Assogastecnici that this score is correct since DMF is not a PBT or vPvB substance. DMF is considered to be a SVHC only on the basis of "hazard to the unborn child" (H360D). • Assogastecnici has no comments about the total	Thank you for your comment. **WDU score** Please refer to response to comment 2488.

			DMF quantity used in Europe stated by ECHA (100,000 to 120,000 tonnes per year that led to a score of 9 i.e. highest available score). • DMF exposure routes has been scored as 3x3=9 i.e. highest available score. Assogastecnici has no information about the score 3 for "Uses in industrial settings at a high number of sites". Assogastecnici questions the score 3 for "Significant potential for worker exposure from uses within the scope of authorisation" on the basis that the uses described in the prioritisation document are industrial and indirect contact i.e. closed processes. On this basis a scoring factor of 0 or 1 would be the correct worker exposure value. That would make the exposure route score 0 or 3 and the total score 9 or 12 instead of 18. That will reduce the priority placed upon DMF in the selection from the candidates list	
2295	2013/09/20 10:40	Federchimica, Industry or trade association, Italy	The substance has specific uses for which there are not potential alternatives with a lower hazard profile. Commission Directive 2009/161/EU of 17 December 2009 established the IOEL for DMF to be 15 mg/m3 (TLV-TWA) and 30 mg/m3 (TLV-STEL). We think that the IOELS values should be considered as binding values, and therefore should be accepted as a minimum requirement relating to the protection of human health and the environment for the use of DMF. Accordingly, we believe that the best solution is to attribute binding efficacy to IOELS values (by a directly applicable European regulation, if necessary) and that the uses or categories of uses that comply with Commission Directive 2009/161/EU are exempted from the authorization requirement, as indicated in REACH, Art. 58(2). Moreover, on pag. 15 of the annex XV dossier, there is written that there is no indication of substitution of DMF for its main industrial uses, so we think that the way of Authorization is a disproportionate measure for this substance and not the most appropriate Risk Management Option (RMO) for save uses. Consequently, and only in case it won't be accepted the IOELS values as binding values, we believe that it would be better to address the DMF in the process of restriction; in this way, the uses for which there are no substitutes and can	Thank you for your comment. **Other RMO, imported articles** Please see response to comment 2427. **Exemption 58(2), No suitable alternatives, No risks for specific application** Please see response to comment 2455 and 2456. **Authorisation disproportionate as no alternatives** Although the substance is of economic importance and apparently difficult to substitute in a range of its uses, it is also toxic to reproduction. Hence there is as well a strong societal interest to protect humans, in particular workers handling the substance, from risks potentially arising from its uses. Taking account of these conflicting areas, authorisation can be considered as being an appropriate risk management measure. It does not 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

			be documented as safe in industrial processes, will be preserved. Another consideration concerns the statement on pag. 8, in which there is the notice that the largest consumer of DMF in the world is China; we think that the eventually future band of DMF, derived from the process of authorization, will not resolve the problem of articles with DMF put on the European market by Chinese manufacturers. As a matter of fact, the process of restriction would allow a greater control on finished articles coming from outside Europe. In addition, on the economical side, it has to be considered that the impact on some industries would be very high. In particular, if the DMF will be inserted in annex XIV of REACH, several manufacturings will close and many downstream users (in particular for the production of articles) will have problems to continue their activities. On the scoring: Federchimica challenges the scoring that has justified this prioritisation: • DMF has scored 0 (lowest possible) in terms of its inherently hazardous properties. This appears corrects as DMF is not a PBT or vPvB substance. DMF qualifies to be considered for SVHC only on the basis of "hazard to the unborn child" (H360D). • DMF exposure routes has been scored as 3x3=9 (highest available score). Sites The data in our possession show that the number of sites is very limited compared to other chemicals. Differently from what is stated in ECHA's draft background document, DMF is not used throughout the EU at hundreds of use sites, since we believe the number of sites is much lower. Therefore the score equal to 3 doesn't appear rightful, in our opinion the score should be 1. Release In addition, a score equal to 0 (insignificant) would be more appropriate for "significant potential for worker exposure from uses within the scope of authorisation", on the basis that the uses of DMF are controlled, safe and not widespread (industrial only). DMF is used in closed units, under suction systems, stored in closed	for are properly controlled or that there are no alternatives available and the socio-economic . benefits are outweighing the risks arising from the uses. Concomitantly, the obligation to apply for authorisation is a strong incentive (or duty) to search for and develop suitable alternatives. **WDU Scoring** Further justification on how DMF fulfils the criteria listed in Article 58 (3) is provided in the response to comment 2488.

			vessels, transported and used under strictly controlled conditions. Exposure of workers in is regulated (IOEL) and personnel handling DMF in industry is well educated. Furthermore we believe that the use of DMF is wide spread and not wide dispersive. Wide-dispersive uses are characterised by use(s) of a substance on its own, in a preparation or in an article at many places (sites) that may result in releases and exposure to a considerable part of the population (workers, consumers, general public) and/or the environment. This means that uses taking place at many places, which however do not result in significant releases of a substance, may be considered only as 'widespread' but not as 'wide-dispersive'. With regard to the DMF risk management measures are in place to control workplace exposure and emissions to the environment. Hence we can not agree that a score of 9 is given to "wide dispersive use". Consequently the overall score is 9 = IP + v + WDU= 0 + 9 + (1*0).	
2294	2013/09/20 10:29	Individual, Italy	See our attachment in the confidential section	Thank you for your comment. **Risk controlled, No suitable alternative** Please see response to comment 2455. **Authorisation perceived as a ban / socioeconomic considerations** Please note that use of DMF 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. 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.
2291	2013/09/20	CIRFS; European Man-made	The use of substances being handled in compliance with regulatory limits is to exempt from the approval	Thank you for your comment.

	10:25	Fibres Association, Industry or trade association, Belgium	procedure under REACH. For the substance N, N-Dimethylformamide there is a European limit (iOEL), that has been implemented in the Member States in accordance with Directive 2009/161/EC of 17 December 2009. Compliance with the respective national limit values meeting is sufficient for an exemption according Article 58 (2) of the REACH Regulation, as there is no legal vacuum without authorization. In Germany, for example, compliance with the occupational exposure limit values laid down in the German labour law; the technical rules for dangerous substances (TRGS), fixed occupational exposure limit values (AGW) or biological limit values (BGW) in accordance with TRGS 900 or TRGS 903, is seen as sufficient to obtain an exemption.	**Exemption 58(2)** Please see response to comment 2456.
2290	2013/09/20 09:29	Company, Belgium	We support completely the comments of 'Fedustria' on ECHA's recommendation to include DMF in the Authorisation List. The fact that DMF will be prioritised for authorisation and that no valuable alternative is available, leads to high levels of uncertainty within the textile coating companies, as authorisation is by definition limited in time. We will have to face significant costs involved by the application for this authorisation. In other words, it will result in an additional impediment of the competitiveness with regard to the non-European enterprises. Moreover, this uncertainty will curb every additional investment in Belgium. Contrary to authorisation, restriction can apply to EU produced goods (articles) as well as to imported goods. It should be noted that authorisation will have as consequence that production will relocate towards non-EU countries. As in those countries there is no such stringent legislation, one may fear that goods that will be imported in the EU might not be REACH-conform and might as consequence pose a risk for the consumer. Therefor restriction on article level is a better measure to protect the consumer and to guarantee a level playing field. Authorisation will not bring any added value to the requirements already imposed by the VOC-Directive 1999/13/EC and the Directive 2009/161/EC (on occupational exposure limits) establishing a indicative occupational exposure limit value for DMF for the protection of workers from chemical risks. In confidential	Thank you for your comment. **High level of uncertainty / Competitive disadvantage / Relocation outside EU** Please refer to response to comments 2488 and 2415. **Other RMO, imported articles, no alternative** Please refer to response to comment 2427. **Added value of the authorisation process** Please refer to response to comment 2340. **DMF use pattern in specific industrial sectors/company** Please refer to response to comment 2456.

			attachments 'Labo2011/2012' you can find the results of biomonitoring on all our well trained workers and there is no problem at all. In the textile coating industry DMF is only used in an industrial setting under controlled conditions (environment and protection for worker exposure). In order to minimize the emissions to the environment below the emission limits the substance DMF is recovered by scrubber distillation in a closed loop system. The remaining emissions are treated in a solvent after burner. In confidential attachments 'DMF2011/2012' you will see that our emissions of DMF are below 2mg/Nm3. So we can conclude that , with all the investments that have already been made and the arrangements that have been taken, we fulfil all the requirements for a safe use of DMF. Consequently an additional Reach legislation will not increase safety of workers nor the quality of the environment.	
2289	2013/09/20 09:13	Company, Germany	please see V - confidential attachment	Thank you for your comment and the information provided.
2286	2013/09/19 20:35	Company, Ireland	Allergan Pharmaceticals Ireland requests that the use of DMF in the manufacturing of pharmaceutical 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 is exempted from REACH authorisation requirements. This exemption would also include all PPORD uses of DMF (up to 50ts/pa) in the production of medicinal and veterinary products. We believe this exemption should be granted because of the following key reasons: • Community Legislation relating to the Health, Safety and Environmental (HSE) control of DMF already exists in particular community legislation relating to Occupational Exposure Levels. • Community Legislation covering substitution/replacement of DMF already exists under the Industrial Emissions Directive; • Use of DMF in pharmaceutical manufacturing is	Thank you for your comment. **Exemption 58(2)** Please see response to comment 2456.

			not wide dispersive • If technically possible at all (see reasoning below), DMF can only be substituted by other Aprotic Solvents with similar health hazards; • Substituting a solvent used in the manufacture of a commercially available Pharmaceutical Product may require additional human and animal testing (contrary to the principles of REACH); • Substituting a solvent used in the manufacture of a commercially available Pharmaceutical Product requires the current Marketing Authorisations (granted by the European Medicines Agency (EMA)) to be amended leading to excessive costs (3M – 12M EUR per product) and time delays; • REACH article 62(5)(b)(i) suggests that an Annex XIV listed substance handled in a facility that is permitted by Directive 96/61/EC doesn't need to consider risks from Human Health or the Environment when submitting an application for an Authorisation Use of that Substance	
2285	2013/09/19 19:45	Individual, France	Diagnostica Stago wishes to comment on public consultation relating to a product made with DMF. See attachment confidential document.	Thank you for your comment. **Disruption of market if supplier doesn't apply for authorisation** Please see response to comment 2455.
2284	2013/09/19 19:31	Individual, France	Diagnostica Stago wishes to comment on public consultation relating to DMF. See attached confidential document.	Thank you for your comment See response to comment 2285.
2283	2013/09/19 19:27	Company, Portugal	Endutex manufactures coated fabrics with PVC, PU and other polymers. Endutex uses Polyurethane (PU) solutions that contain DMF as a solvent. These PU solutions are used to produce synthetic/artificial leather. This synthetic/artificial leather is sold to other companies (mainly inside EU) to manufacture a range o articles as: - Clothing (rainwear, cold wear, …) - Protective suits - Mattress protection - Automobile Leather like products - Upholstery Endutex is concerned that the inclusion of DMF in the authorisation process will lead to an increase of prices in	Thank you for your comment. **Permanent competitive disadvantage and proportionality of the authorisation process** See response to comment 2488.

			EU, resulting in decrease competitiveness and losing business. Particularly in favour of imports from non EU countries. (Especially from China). If this trend is not stopped, EU industry will continue to disappear, with all the social consequences.	
2282	2013/09/19 19:27	Taminco BVBA, Company, Belgium	Comments on ECHA's Prioritization of recommending N,N-Dimethylformamide (CAS 68-12-2, DMF) for Annex XIV inclusion through the 5th Priority List for Authorisation This document reflects the concerns and objections of Taminco BVBA on ECHA's recommendation for including DMF into REACH Annex XIV for Authorisation. Taminco is a major EU manufacturer of DMF and is acting as the Lead Registrant, consequently has submitted the Lead REACH Registration Dossier on behalf of the DMF registrants. Our comments are based on ECHA's "Draft background document for N,N-Dimethylformamide, dated 24th of June 2013 (in the following "Draft Prioritisation Document"). Summary and general comments Authorisation would be a disproportionate provision and therefore is not the most appropriate Risk Management Option (RMO) for safe use of DMF in the EU. The substance is used in industrial processes, where the risks are already adequately controlled and uses are safe, in particular because EU-wide DMF legislation on safe management exists. Therefore, the most proportional, appropriate and straightforward way of ensuring the safe use of DMF is to enforce the already existing Occupational Exposure Limit (OEL), coupled with restrictions for articles, which might contain DMF as impurity. As a fallback position, we would as well support the Restriction of "risky" uses (where safe use according to the existing OEL cannot be documented) or the Exemption of industrial solvent use, based on the existing EU-wide OEL. The goal should be to eliminate any possible health risks but prevent a general elimination of DMF by Authorisation for proven safe industrial processes, where existing EU legis¬lation (and industry standards) already properly controls the risks. Manufacturers outside the EU and companies importing manufactured articles into the EU would not be affected by the authorisation requirements, which could lead to a	Thank you for your comment and the information regarding update of registration. Please see response to comment 2488. **Other RMO, imported articles, consistent approach with similar solvent** See response to comment 2427. **Added value of the authorisation process** Please refer to response to comment 2340. **Exemption art 58(2)** Please consider response to comment 2456. In addition, as stated, DMF is restricted in accordance with entry 30 of Annex XVII of the REACH Regulation. Pursuant to entry 30 of Annex XVII of REACH Regulation substances which appear in Part 3 of Annex VI to Regulation (EC) No 1272/2008 (CLP Regulation) classified as toxic to reproduction category 1A or 1B (Table 3.1), shall not be placed on the market, or used, as substances, as constituents of other substances or in mixtures, for supply to the general public when the individual concentration in the substance or mixture is equal to or greater than either the relevant specific concentration limit specified in Part 3 of Annex VI to the CLP Regulation, or the relevant concentration specified in Directive 1999/45/EC where no specific concentration limit is set out in Part 3 of the CLP Regulation. Article 56(6)(b) of REACH provides that the authorisation requirement does not apply to the use of substances when they are present in

			permanent competitive disadvantage for EU industry. This is disproportionate and a competitive disadvantage for a manufacture in the EU. However REACH Article 1(1) states that REACH has the aim to enhance competitiveness. The principle of proportionality is laid down in Article 5 of the Treaty on the European Union. Comments to Section 2.2.2.2. Uses and releases from uses Uses: ECHA's Draft Prioritisation Document is referencing to our opinion non-registered uses, which were taken most likely from the open literature (if these referenced uses are not registered confidential uses, not visible for the lead registrant). Non-registered uses are according to REACH (Article 14 and 37) not allowed and should therefore not be relevant in a Prioritisation Document. In our role as Lead Registrant, we are currently in the process of updating the Chemical Safety Report (CSR) with up-to-date information on uses and exposure. We are inviting ECHA to review the updated CSR as soon as we have conducted the spontaneous dossier update. Moreover, we are happy to include uses, which pose a concern to ECHA and which have not been included in the Risk Assessment of the Lead Dossier, as "Uses Advised Against". Any downstream user which wants to continue with uses advised against would then need to provide information and evidence on the safe use of these applications to ECHA. Furthermore, ECHA is raising concerns with regard to presence of DMF in articles. When the substance is used as industrial process solvent, it is removed at the end of the process and consequently downstream users and consumers cannot be exposed. Moreover, impurities of chemicals in articles cannot be regulated by the REACH Authorisation process and have to be restricted by the REACH Restriction process. Releases: DMF is a threshold chemical; a threshold is the exposure level or dose of an agent, above which toxicity or adverse health effects can occur, and below which toxicity or adverse health effects are very unlikely. The threshold derivation is a scientific assessment based on the known toxicity and information of a chemical. The	mixtures below the lowest of the concentration limits specified in Directive 1999/45/EC or in Part 3 of Annex VI to the CLP Regulation. DMF was identified as a Substance of Very High Concern (SVHC) according to Article 57 (c) REACH as it is classified in Annex VI, Part 3, Table 3.1 of CLP Regulation as toxic for reproduction, Repr. 1B, H360D ("May damage the unborn child"), and was therefore included in the Candidate List for authorisation on 19 December 2012, following ECHA's decision ED/169/2012. Table 3.1 in Part 3 of Annex VI to CLP Regulation does not set out a specific concentration limit; thus, the concentration limit specified in Directive 1999/45/EC applies. Accordingly, the concentration limits specified for DMF in Annex XVII of REACH are in fact the same as the concentration limits referred to in Article 56(6)(b) REACH. Therefore, the use of DMF below the concentration limits set out in Annex XVII of REACH does not need to be subject to an exemption from authorisation. **Competitive disadvantage, proportionality of the authorisation process, WDU score, Threshold, Risks controlled due to existing legislation, No suitable alternatives, Socioeconomic considerations** Please consider response to comments 2488 and 2455. **Prioritisation approach is currently under revision.** As stated in the prioritisation results table, and as it had been discussed with the MSC before preparing the recommendation, the prioritisation for this year was made according to the currently agreed general approach document available at: (http://echa.europa.eu/docu+E2ments/10162/17232/axiv_priority_setting_gen_approach_20100701

			threshold limit value (TLV) is a level to which it is believed a worker can be exposed day after day for a working lifetime without adverse health effects. Based on the threshold limit value, the EU has implemented an EU-wide Occupational Exposure Limit (OEL) for DMF, which has been set with 5 ppm for an 8 hour average respectively with 10 ppm for a 15 min short-term exposure. Accordingly, it is not necessary, that the exposure to DMF has to be "zero". DMF is used exclusively in industrial processes where the risks are already adequately controlled and uses are safe. The only non-industrial use is in professional laboratories (which often belong to industrial settings), where strict occupational controls and chemical hygiene procedures are applied, since the handling of hazardous chemicals is day-to-day routine for this profession. Most of the analytics is related to Research & Development, a use which is by definition (REACH Articles 2 and 56) exempted from Authorisation. Thus, this use should not be factored into the prioritization considerations at all. The OEL, as set by the EU, has to be implemented as minimum requirement by each EU Member States. All DMF manufactures and users have to apply this value, which is proven to be safe. According to our evaluation, 20 of the 28 Member States (including Croatia) have implemented the indicated OEL and we are really wondering, why the Commission is not enforcing the implementation at Member State Level. In our function as lead registrant, we are currently in the process of compiling additional data on exposure, comprising for example measured data (e.g. air concentrations), process descriptions and operational conditions in the different applications and uses included in the lead dossier. This data will be utilized to update the CSR of DMF. Conclusion: Taminco disagrees that potential for significant exposure exists. The updated CSR will address this concern by including more detailed information on Use, Release and Exposure. Comments to Section 2.3. Availability of information on alternatives As correctly pointed out by ECHA, potential alternatives, that are to some extent interchangeable, are other	en.pdf). In general, approaches are always subject to improvements and adaptations. The fact that there are ongoing discussions for updating the general prioritisation approach does not mean that ECHA should refrain for prioritising substances until an updated approach is agreed.

			aprotic solvent of medium polarity, which all carry the same intrinsic properties with regards to reproductive toxicity. Some of these substances are already on the Candidate List (NMP, DMAC). While SVHC substitution and replacement of CMRs is desirable, finding of alternatives to aprotic solvents of medium polarity has been rather unsuccessful, even after 20 years of research work. In most of the EU Member States the substitution principle of very toxic or CMR substances is manifested since years in their respective chemical control legislation (e.g. German "Gefahrstoffverordnung"), so looking for alternatives on aprotic solvents is nothing new. According to the responses we get from our downstream users, DMSO is not a suitable alternative, as pointed out by ECHA. This became as well evident from the downstream user comments received during the ANNEX XV Dossier consultations (identification of a substance as SVHC) on DMF, DMAC and NMP. Therefore, it is difficult to understand why for some substances (e.g. NMP) restrictions were proposed, while this was not the case for DMF and DMAC, subverting a coherent handling of very similar substances with equal conditions, undermining the consistency of chemical management under REACH Regulation. Additionally, substitution is economically not viable in many applications. Considerable socio-economic impact would result for uses with long-term approval procedures, after implementing new processes and materials used. Comments to Section 2.4. Existing specific Community legislation relevant for possible exemption We disagree with the ECHA position, that there seems to be no specific Community legislation in force, that would allow considerations of exemptions of uses from the authorisation requirements on the basis of Article 58(2) of the REACH Regulation. DMF is used in industrial processes where the risks are already adequately controlled and uses are safe for the below mentioned reasons: ☐ * DMF is included in 3rd list of indicative occupational exposure limit values (IOELVs) set up by Commission Directive 2009/161/EU (17.12.2009). IOELVs are health-based values derived from the most	

			recent scientific data and correspond to threshold levels of exposure below which no detrimental effects are expected after short-term or daily exposure to the substance over a working life time. Member States were required to establish a national OEL, taking into account the Community limit value of DMF by 18 December 2011. Directive 2009/161/EU properly addresses the occupational use of DMF and health risk in connection with its use. ☐ * EU legislation, like Council Directive 98/24/EC (Protection of health and safety of workers from risks related to chemical agents at work) and Council Directive 92/85/EEC (Measures to encourage improvements in the safety and health at work of pregnant workers and workers who recently given birth or are breastfeeding), provide further measures, which ensure a safe use of reprotoxic substance like DMF. ☐ * REACH Article 62 (5b) states that emissions of a substance (VOC) from an installation for which a permit was granted in accordance with Directive 96/61 can be omitted in an authorization dossier. Indirectly (via emissions of an industrial installation) this in an exemption of VOC caused by industrial use from authorization requirement based and on existing EU legislation as demanded by REACH 58.2. DMF use in an industrial installation has to be approved by granting of an authority permit in accordance with Directive 96/61 already. ☐ * DMF consumer-use is restricted according to Annex XVII of REACH regulation (Restriction No. 30). DMF is explicitly listed in the appendix 6 which specifics restriction No. 30 to be mandatory for DMF as existing specific EU regulation/legislation. In conclusion, there is specific community legislation in place which would justify an exemption according to REACH Article 58.2, when DMF is used as industrial process solvent. Comments to Section 3.1. Prioritisation Due to high volume, wide dispersive use and large number of use sites, a high score (18) was derived by ECHA on DMF prioritization. The number of industrial sites using DMF in industrial processes in high volumes is limited and emission controls are in place. Consequently, most of the DMF	

			tonnage consumed in the EU is used at a small number of sites. The majority of the sites using DMF are laboratories, which utilize marginal quantities. R&D Laboratories should not be considered for priority scoring and excluded from the number of sites. It is highly questionable if the real exposure matches the wide-dispersive use criterion. Wide-dispersive uses are characterised by use(s) of a substance at many sites that may result in significant releases and exposure to a considerable part of the population (workers, consumers, and general public) and/or the environment. It can be demonstrated with exposure data, that risks are adequately controlled in industrial settings. It seems that the score for DMF is so high, as if professional and even consumer uses have been included in the scoring calculation. Consequently, the scoring does not reflect that the DMF use is industrial only. Moreover, it is our understanding that ECHA is proposing to reopen the discussion on the prioritization criteria, because practical experience has clearly shown that a refinement of the criteria is necessary. We therefore recommend that the scoring of DMF is being re-done, based on real use and release information and according to the newly developed prioritization criteria. In particular, more recognition should be given that DMF is not meeting the "wide dispersive use" criteria and real exposure/release information of the substance should be taken into account. Therefore, the Prioritisation Score of 18 is highly overrated.	
2279	2013/09/19 18:23	Company, Italy	Please, see below in the Confidential section our comments and Attachments.	Thank you for your comment. **Added value of the authorisation process** Please refer to response to comment 2340. **Risk controlled, no alternative** Please refer to response to comment 2455. **Competitive disadvantage** Please refer to response to comment 2488. **Imported articles** See response to comment 2427.

2278	2013/09/19 17:57	Company, Belgium	We believe that textile coating as described in annex I of the directive 1999/13/EC)should be exempted from authorization for the reasons described in the attachment ECHA_DMF.pdf	Thank you for your comment. **Exemption Art 58(2)** Please see response to comment 2456. **Prioritisation, no added value of authorisation requirement, uncertainty, distortion, competitive disadvantage, delocalisation** Please see response to comments 2488 and 2415. **Other RMO, consistent approach with similar solvent, imported articles** See response to comment 2427.
2276	2013/09/19 17:29	Company, Germany		-
2273	2013/09/19 16:05	EURATEX, Industry or trade association, Belgium	The use of DMF in textile coating should be exempted from authorisation as there is sufficiently specific Community legislation that covers this use and the risks are adequately controled. restriction on article level is a better measure to protect the consumer and to guarantee a level playing field. In the textile coating industry DMF is only used in an industrial setting under controlled conditions. Despite several years of investigation, no valuable alternative to replace DMF has been found to this day. specific Community legislation is in force that would allow exemption of use from the authorisation requirement on the basis of Article 58(2) of the REACH Regulation	Thank you for your comment. **Exemption Art 58(2)** Please see response to comment 2456. **Prioritisation, no added value of authorisation requirement, uncertainty, distortion, competitive disadvantage, delocalisation** Please see response to comments 2488 and 2415. **Other RMO, consistent approach with similar solvent, imported articles** See response to comment 2427.
2261	2013/09/19 13:53	Individual, Italy	See the uploaded attachment	Thank you for your comment. **No alternative, risk controlled** Please refer to response to comment 2455. **DMF use pattern in specific industrial sectors/companies** Please refer to response to comment 2456.
2259	2013/09/19 13:38	Norway, Member State	The Norwegian CA supports the prioritisation of N,N-dimethylformamide (DMF) for inclusion in Annex XIV	Thank you for providing your opinion.
2255	2013/09/19 12:39	Sweden, Member State	We support the prioritisation N,N-dimethylformamide for inclusion in Annex XIV. The substance has high priority	Thank you for providing your opinion.

			due to very high volume and wide dispersive use.	
2246	2013/09/18 16:38	The Linde Group, Region Central and Northern Europe, Company, Germany	Dear Ladies and Gentlemen, In behalf of the Linde Group, Region Continental and Northern Europe, I want to confirm the formal response from the EIGA. Ralf Thomaschewski Acetylene Production Manager - RCNO Region Continental & Northern Europe Linde AG Linde Gases Division, Reisholzer Bahnstraße 4, 40599 Düsseldorf, Germany Phone: +49.211.7481.110, Mobil +49.172.5721477 ralf.thomaschewski@de.linde-gas.com, http://www.linde-gas.de Sitz der Gesellschaft: München, Registergericht: München, HRB 169850 Aufsichtsrat: Manfred Schneider (Vorsitzender), Vorstand: Wolfgang Reitzle (Vorsitzender), Aldo Belloni, Tom Blades, Georg Denoke, Sanjiv Lamba Registered Office: Munich/Germany, Court of Registration: Munich, HRB 169850 Supervisory Board: Manfred Schneider (Chairman), Executive Board: Wolfgang Reitzle (Chairman), Aldo Belloni, Tom Blades, Georg Denoke, Sanjiv Lamba On the scoring: EIGA notes that DMF having scored 18 out of a possible 27, has been prioritised as at least sixth (now fifth as one other substance has been removed from the 2013 priority list) out of one hundred and forty four substances on the candidates list. EIGA challenges the scoring that has justified this prioritisation. • DMF has scored 0 (lowest possible) in terms of its inherently hazardous properties This appears corrects as DMF is not a PBT or vPvB substance. DMF qualifies to be considered for SVHC only on the basis of "hazard to the unborn child" (H360D). • DMF quantity used in Europe is stated as 100,000 to 120,000 tonnes per year and scored as 9 i.e.	Thank you for your comment. Please refer to response to comment 2152.

			highest available score. EIGA cannot comment on the total usage in Europe, this should be data sourced from the manufacturers. • DMF exposure routes have been scored as 3x3=9 i.e. highest available score. EIGA cannot comment on the 3 for "Uses in industrial settings at a high number of sites". EIGA does challenge the 3 for "Significant potential for worker exposure from uses within the scope of authorisation" on the basis that all of the uses described in the prioritisation document are industrial and indirect contact i.e. closed processes EIGA's experience is that worker exposure is a lot less than as described in the prioritisation document, where it says exposure is >4hrs/day and <240 days per year (see Attachment in Section 4). On this basis a scoring factor of 0 or 1 is the correct worker exposure value. That would make the exposure route score 0 or 3, instead of 9. This would make the total score 9 or 12 instead of 18. That will reduce the priority placed upon DMF in the selection from the candidates list.	
2241	2013/09/18 14:58	Air Liquide Deutschland GmbH, Company, Germany	On the scoring: Air Liquide Deutschland GmbH notes that DMF having scored 18 out of a possible 27, has been prioritised as at least sixth (now fifth as one other substance has been removed from the 2013 priority list) out of one hundred and forty four substances on the candidates list. EIGA challenges the scoring that has justified this prioritisation. • DMF has scored 0 (lowest possible) in terms of its inherently hazardous properties This appears corrects as DMF is not a PBT or vPvB substance. DMF qualifies to be considered for SVHC only on the basis of "hazard to the unborn child" (H360D). • DMF quantity used in Europe is stated as 100,000 to 120,000 tonnes per year and scored as 9 i.e. highest available score. Air Liquide Deutschland GmbH cannot comment on the total usage in Europe, this should be data sourced from the manufacturers. • DMF exposure routes has been scored as 3x3=9 i.e. highest available score.	Thank you for your comment. Please refer to response to comment 2152.

			Air Liquide Deutschland GmbH cannot comment on the 3 for "Uses in industrial settings at a high number of sites". Air Liquide Deutschland GmbH does challenge the 3 for "Significant potential for worker exposure from uses within the scope of authorisation" on the basis that all of the uses described in the prioritisation document are industrial and indirect contact i.e. closed processes Air Liquide Deutschland GmbH experience is that worker exposure is a lot less than as described in the prioritisation document, where it says exposure is >4hrs/day and <240 days per year (see Attachment in Section 4) On this basis a scoring factor of 0 or 1 is the correct worker exposure value. That would make the exposure route score 0 or 3, instead of 9. This would make the total score 9 or 12 instead of 18. That will reduce the priority placed upon DMF in the selection from the candidates list	
2240	2013/09/18 14:50	Air Liquide Deutschland GmbH, Company, Germany	On the scoring: Air Liquide Deutschland GmbH notes that DMF having scored 18 out of a possible 27, has been prioritised as at least sixth (now fifth as one other substance has been removed from the 2013 priority list) out of one hundred and forty four substances on the candidates list. EIGA challenges the scoring that has justified this prioritisation. • DMF has scored 0 (lowest possible) in terms of its inherently hazardous properties This appears corrects as DMF is not a PBT or vPvB substance. DMF qualifies to be considered for SVHC only on the basis of "hazard to the unborn child" (H360D). • DMF quantity used in Europe is stated as 100,000 to 120,000 tonnes per year and scored as 9 i.e. highest available score. Air Liquide Deutschland GmbH cannot comment on the total usage in Europe, this should be data sourced from the manufacturers. • DMF exposure routes has been scored as 3x3=9 i.e. highest available score. Air Liquide Deutschland GmbH cannot comment on the 3 for "Uses in industrial settings at a high number of sites". Air Liquide Deutschland GmbH does challenge the 3 for "Significant potential for worker exposure from uses	Thank you for your comment. Please refer to response to comment 2152.

			within the scope of authorisation" on the basis that all of the uses described in the prioritisation document are industrial and indirect contact i.e. closed processes Air Liquide Deutschland GmbH experience is that worker exposure is a lot less than as described in the prioritisation document, where it says exposure is >4hrs/day and <240 days per year (see Attachment in Section 4) On this basis a scoring factor of 0 or 1 is the correct worker exposure value. That would make the exposure route score 0 or 3, instead of 9. This would make the total score 9 or 12 instead of 18. That will reduce the priority placed upon DMF in the selection from the candidates list	
2237	2013/09/18 12:17	Industrievereinigung Chemiefaser e. V. , Industry or trade association, Germany	Die Verwendung von Stoffen, die unter Einhaltung gesetz-licher Grenzwerte gehandhabt werden, ist vom Zulassungs-verfahren nach REACH auszunehmen. Für den Stoff N,N-Dimethylformamid gilt gemäß Richtlinie 2009/161/EU vom 17. Dezember 2009 ein europäische Richtgrenzwert (iOEL), der innerhalb einer Frist in den Mitgliedsstaaten umzusetzen war. Die Einhaltung der jeweiligen nationalen Grenzwerte ist ausreichend, um dem entsprechenden Unternehmen/Betrieb die Ausnahmeregelung nach Art. 58 (2) REACH zu gewähren, da es auch ohne Zulassungspflicht keinen rechtsfreien Raum gibt. Für Deutschland z. B. muss die Einhaltung der im deutschen Arbeitsrecht in den Technischen Regeln für Gefahrstoffe (TRGS) verankerten Arbeitsplatzgrenzwerte (AGW) oder Biologischen Grenzwerte (BGW) gemäß der TRGS 900 bzw. der TRGS 903 hinreichend für den Erhalt einer Ausnahmeregelung sein.	Thank you for your comment. **Exemption Art. 58(2)** Please see response to comment 2456.
2236	2013/09/17 19:57	Pharmachemical Ireland, Industry or trade association, Ireland	Pharmachemical Ireland (PCI) requests that the use of DMF in the manufacturing of pharmaceutical 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 is exempted from REACH authorisation requirements. This exemption would also include all PPORD uses of DMF (up to 50ts/pa) in the production of medicinal and veterinary products. We believe this exemption should be granted because of	Thank you for your comment. **Exemption** Please see response to comment 2456.

			the following key reasons: • Community Legislation relating to the Health, Safety and Environmental (HSE) control of DMF already exists in particular community legislation relating to Occupational Exposure Levels. PCI members have DMF OEL monitoring data taken from various Active Pharmaceutical Ingredient (API) Manufacturing facilities across the state that can be shared with ECHA on request from ECHA; • Community Legislation covering substitution/replacement of DMF already exists under the Industrial Emissions Directive; • Use of DMF in pharmaceutical manufacturing is not wide dispersive • If technically possible at all (see reasoning below), DMF can only be substituted by other Aprotic Solvents with similar health hazards; • Substituting a solvent used in the manufacture of a commercially available Pharmaceutical Product may require additional human and animal testing (contrary to the principles of REACH); • Substituting a solvent used in the manufacture of a commercially available Pharmaceutical Product requires the current Marketing Authorisations (granted by the European Medicines Agency (EMA)) to be amended leading to excessive costs (3M – 12M EUR per product) and time delays; • REACH article 62(5)(b)(i) suggests that an Annex XIV listed substance handled in a facility that is permitted by Directive 96/61/EC doesn't need to consider risks from Human Health or the Environment when submitting an application for an Authorisation Use of that Substance The amount of DMF manufactured and/or imported into the EU is, according to registration data, in the range of 10,000 – 100,000 t/y. No information on exports is provided. According to registration information complemented by information from industry consultations performed in 2011 and 2012 (Annex XV report, 2012; RCOM, 2012), 50% of the total volume (5,000-50,000 t/y) is used in the production of APIs or crop protection ingredients. The majority of the uses take place at industrial settings. There is no registered use for consumer products.	

			DMF is used within PCI member companies under highly controlled conditions in batch production processes (which typically are run a few times per year/month at most pharmaceutical plants) and is therefore not considered as wide dispersive use nor is there a continuous potential for exposure. Benefits of Aprotic Solvents (such as DMF) in the Production of Medicinal Products DMF is an aprotic solvent used to manufacture Active Pharmaceutical Ingredients (APIs) for pharmaceutical products which treat potentially life threatening or debilitating conditions such as, Small Cell Lung Cancer, Cervical Cancer, Herpes Simplex virus, Varicella Zoster viruse, asthma, eczema and psoriasis. DMF is also used in Pharmaceutical lab R&D and as an analytical standard for a number of medicinal products. The powerful solvating properties of Polar Aprotic Solvents (such as DMF) facilitate organic synthesis reactions which often, cannot be achieved in less polar solvents. Polar Aprotic Solvents offer general high solubility of many APIs and intermediates which often have poor solubility in less polar solvents. This also facilitates processes that require minimal solvent quantities, compared with the much larger volumes of other solvents that may be required. 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 DMF are essential for these reactions, since (a) they prevent unreacted materials from being carried forward in the process stream and (b) they minimise the formation of side products, thereby producing intermediates and APIs of the highest quality. There are other Polar Aprotic Solvents with similar physical or chemical properties (albeit of lower polarity) that could potentially be used in place of DMF in some API manufacturing syntheses. The most common 'direct' alternative may be DMAC. Others include formamide, N-methylformamide, NMP, NEP and N-methylacetamide. However, these alternatives carry essentially the same health hazard as DMF. Some of these solvents are already on the REACH Candidate List or have been proposed to Annex XIV or Restriction. In addition, these solvents may have different reactivity and so the	

			replacement of DMF with such solvents could lead to incomplete reactions and side products that impact the safety, quality and yield of the API. Moreover, this may result in additional animal and human testing and waste streams. In other cases, the properties of DMF are so unique in effecting a desired reaction reactivity, selectivity, solubility, or purification that no comparable performance with any other solvent is known or the alternative solvents pose a greater environmental, occupational health, or other concern. Work to identify alternatives to DMF in the manufacture of pharmaceutical products within the EU has been undertaken in the past with very limited success. Significant development work would be required to identify and validate viable alternatives involving major changes to the manufacturing processes and the Marketing Authorisation. Given the complexity of global supply chains, the ability of the pharmaceutical industry to secure a continuous supply of medicines to the market could be at risk if DMF was not available for use. Description of the Use of DMF in the Production of Medicinal Products The manufacture of APIs and associated intermediates are performed in enclosed reactor trains in accordance with Good Manufacturing Practices (GMP). DMF (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). Residual amounts of DMF in the eventual pharmaceutical product are safety-limited by the ICH Q3C (Guideline for Residual Solvents). So in practice, virtually all the DMF used during manufacture would be present in the waste streams (other than that lost through evaporation) which is primarily disposed of via incineration (some recycling of DMF will occur). Altogether, the risks of environmental exposure of DMF in the pharmaceutical manufacturing environment are minimized by the equipment design and operational controls.	
2234	2013/09/17	Fedustria, Industry or trade	Fedustria is the federation of the Belgian textile, wood	

	16:11	association, Belgium	and furniture industries and represents consequently the Belgian textile coating companies. The Belgian textile coating companies have specialised in polyurethane coating and have thus acquired a unique position in Europe. Thanks to this specific coating technology, these enterprises are capable of developing high-quality, demanding textile products that are mainly used in medical and highly technological fields such as protective clothing. The specific requirements essential to such applications, e.g. chemical resistant to cleaning and disinfection, thermoplastic behavior, etc. can only be realised by (aromatic) polyurethane coating for which DMF is an essential solvent. The use of DMF in textile coating should be exempted from authorisation as there is sufficiently specific Community legislation that covers this use and the risks are adequately controlled. The reason for this exemption is extensively described in the section "uses exempted for authorisation". Nevertheless we want to give some general comments on the overall approach described in the draft background document for the prioritisation for DMF. Same approach for all aprotic solvents needed Like most of the aprotic solvents, DMF is classified as a reprotoxic substance (Rep. Cat. 1B). At this moment, different aprotic solvents (DMF, NMP, DMAC) are treated in a different way under REACH. Some are considered under the restriction procedure (e.g. NMP), others are proposed to be handled under authorisation (DMF, DMAC). However there is no scientific logic to handle very similar solvents under different regulatory approaches. Both the industry and many authorities are the opinion that it would be more logical and consistent to treat all aprotic solvents in an identical way (e.g. all under restriction). Level playing field … also for imported goods Authorisation will not bring any added value to the requirements already imposed by the VOC-Directive 1999/13/EC and the Directive 2009/161/EC (on occupational exposure limits) establishing a indicative occupational exposure limit value for DMF for the protection of workers from chemical risks. Contrary to authorisation, restriction can apply to EU produced goods (articles) as well as to imported goods.	Thank you for your comment. Please see response to comment 2278.

			It should be noted that authorisation will have as consequence that production will relocate towards non-EU countries. As in those countries there is no such stringent legislation, one may fear that goods that will be imported in the EU might not be REACH-conform and might as consequence pose a risk for the consumer. Therefor restriction on article level is a better measure to protect the consumer and to guarantee a level playing field. Prioritization score does not reflect real use in textile coating We can not share the high prioritization score ECHA's draft recommendation (dated 24th of July 2013) calculated for the inclusion of DMF in the Authorisation list. The use of DMF in the textile coating industry is not characterized as being wide-dispersive. In the textile coating industry DMF is only used in an industrial setting under controlled conditions (environment and protection for worker exposure). In order to minimize the emissions to the environment below the emission limits the substance DMF is recovered by scrubber distillation in a closed loop system. The remaining emissions are treated in a solvent after burner. Both technologies fulfill the strict emission limits imposed by both directives. Use to be considered wide-spread instead of wide-dispersive Wide-dispersive uses are characterized by use(s) of a substance on its own, in a preparation or in an article at many places (sites) that may result in significant releases and exposure to a considerable part of the population (workers, consumers, general public) and/or the environment. This means that uses taking place at many places, which however do not result in significant releases of a substance, may be considered only as 'wide-spread' but not as 'wide-dispersive'. With regard to the textile coating, there are a limited number of sites with controlled emissions below the emission limits. Risk management measures are in place to control workplace exposure and emissions to the environment. Hence we cannot agree that a score of 9 is given to "wide dispersive use". As release is controlled (meaning releases at the workplace may occur but that risk management measures are in place to control	

			workplace exposure) the score 1 should be applied for "release", giving an overall score of 3 for "wide dispersive use". This results in a total score of 12 for prioritization, instead of 18 as concluded in the draft background document for DMF. Companies will delocalize in order to avoid distortion of competition The fact that DMF will be prioritised for authorisation and that no valuable alternative is available, leads to high levels of uncertainty within the concerned textile coating companies, as authorisation is by definition limited in time. These enterprises will have to face significant costs involved by the application for this authorisation. In other words, it will result in an additional impediment of the competitiveness with regard to the non-European enterprises. Moreover, this uncertainty will curb every additional investment in Belgium. Potential investors will choose to delocalize new activities outside the EU.	
2233	2013/09/17 15:10	Company, United Kingdom	Ai Products fully endorses the comments made by EIGA	Thank you for your comment. Please see response to comment 2152.
2232	2013/09/17 14:14	Company, Denmark	We recommend restriction over authorisation since we consider restriction to be the best risk management option for N,N-Dimethylformamide, CAS No: 68-12-2 (DMF). We are a manufacturer of high quality active substances used in Plant Protection Products (PPP) and are utilizing DMF as solvent of choice. According to REACH we would be qualifying as a downstream user (DU). Exposure of downstream user, professionals and consumers DMF is classified under GHS as reprotoxic in Cat 1B and is as such already listed in Annex XVII, appendix 6, entry 30. This restricts consumer use both in preparation and as a substance. As declared in the "Draft background document for N,N-Dimethylformamide (DMF)" [hereafter mentioned Draft] there is no registered use for neither consumers nor professionals. The substance is used as an industrial solvent at controlled industrial sites where it is removed from the final product therefore professionals and consumers are not exposed. Exposure of worker	Thank you for your comment. **Other RMO** Please refer to response to comment 2427. **Exemption, competitive disadvantage, uncertainty, proportionality of the authorisation process, relocation outside EU** Please refer to response to comments 2488 and 2415. **No risks, low exposure, no alternatives** Please refer to response to comment 2455. **DMF use pattern in specific industrial sectors/companies** Please refer to response to comment 2456.

			In the Draft it is stated that there is a "significant potential for worker exposure". At our industrial site this is not the case. The substance is used under Strictly Controlled Conditions (SCC) by highly skilled and educated workers using appropriate Risk Management Measures (RMM). In the Draft it is also mentioned that transfer is the most significant potential for exposure but in the paragraph it is the PROC 8a that is mentioned. This regards transfer at non-dedicated facilities but at our site we have dedicated facilities and as such a much lower potential for exposure. Therefore we disagree with the Draft point 3.1. Prioritisation where we believe the score for "Uses – Wide Dispersiveness (WDU)" – "Release" should be lowered since there is not a "significant potential for worker exposure". Measurements of the DMF exposure are done on a regular basis, since this already is required by the authorities. The measured values are found to be far below the occupational exposure limits established by the Commission Directive 2009/161/EU of 17 December 2009 where the IOEL for DMF is 15 mg/m³ (TWA) and 30 mg/m³ (STEL). (Please see the confidential attachment for measurements). This demonstrates that DMF exposure is not a real workplace issue. Substitution An extensive work has been done in order to establish if there are alternatives to DMF. 26 solvents were investigated in more than 120 experiments with a variation of both the alkali and catalyst. A few aprotic polar solvents were found to be almost comparable with DMF in yield, but they turned out to have similar health hazards or other technical problems as indicated below. The use of DMF as solvent results in a very pure end product without neither impurities nor DMF. From a technical point of view DMAc [N,N-dimethylacetamide, CAS No: 127-19-5] is a suitable solvent but it is classified toxic for reproduction category 1B (1272/2008/CE) like DMF and is already on the Candidate list of Substances of Very High Concern and has been prioritised for REACH Annex XIX inclusion.	

			From a technical point of view NMP [n-Methylpyrrolidone, CAS No: 872-50-4] is a suitable solvent but it is classified toxic for reproduction category 1B (1272/2008/CE) like DMF and is already on Annex XVII. HMPT [hexamethylphosphoric triamide, CAS No: 680-31-9] is classified mutagenic in Cat 1B and carcinogenic in Cat 1B and would therefore not be a suitable substitute. Benzene [CAS No: 71-43-2] is very difficult to remove from the final product. In China it is used in the production and here the evaporation takes place in open systems. Benzene is among others classified mutagenic in Cat 1B and carcinogenic in Cat 1A and would therefore not be a suitable substitute. From a technical point of view DMSO [dimethyl sulfoxide, CAS No: 67-68-5] is a suitable solvent although the yield is lower resulting in a higher use of chemicals and increasing waste streams. DMSO has a higher boiling point (198°C) which requires higher operating temperatures (hence more energy) and a mild corrosive nature (requiring stainless steel equipment). It is difficult to regenerate large quantities of DMSO due to thermal instability and there have been reported accidents in the literature. However, the worst concern is that it is not possible to fully remove DMSO from the end product which is a PPP. This would result in a widespread exposure of DMSO on the crops, environment and man. It is worth mentioning that the PPP is used in a number of countries to a number of crops. For every use in every country there is a registration and behind that an evaluation of safe use. If the impurity profile for a PPP changes the PPP Regulation (1107/2009/EU) requires new registrations. This means that a lot of new studies have to be performed and registrations in every country, for every formulation and every crop have to be resubmitted. This is very costly work and will not be feasible. Furthermore a lot of the required studies involve animals and this will go against one of the key principles in REACH; to reduce testing on vertebrate animals. Anti-competitiveness Should DMF end up on the authorisation list with a demand for authorisation also for industrial use it would bring uncertainty for the production at our site. If the	

			authorisation should be taken into consideration every few years it would be difficult to base investment on such a short timeframe. Instead of expanding production here it might lead to a relocation of the whole production to a country outside EU. This could result in a decrease of environmental and working environmental conditions and loss of jobs in the EU. Losing the production of a profitable substance would be difficult for our company and we consider it as a distortion of competition. Conclusion In our case there are no suitable drop-in alternatives for DMF. There is no exposure to professionals or consumers. The exposure to the workers at the industrial setting is low and well below the indicative occupational exposure limit value (IOELV). Since DMF is already subject to an IOELV and additional EU wide risk management measures authorisation would be a disproportionate provision and therefore not the most appropriate risk management option. Instead it would provide a distortion of competition. As an alternative to authorisation we recommend adding DMF to Annex XVII where restrictions could be made towards uses where safe use cannot be documented. If this is impossible we recommend adding DMF to Annex XIV with the exemptions of the industrial uses that can be documented to be safe. Please find further explanation in the field "Uses (or categories of uses) exempted from the authorisation requirement".	
2231	2013/09/17 11:34	Panasonic Industrial Devices Materials Europe GmbH, Company, Austria	DMF is an important solvent for our production process and - at the moment - there are no real technical alternatives due to the special properties of this solvent class. Our products do not contain DMF anymore and are not sold to end users.	Thank you for your comment. **No suitable alternative, risk controlled** Please refer to response to comment 2455. **Authorisation perceived as a ban, plant closure** Please refer to response to comment 2415.
2228	2013/09/17 10:36	United Kingdom, Member State	Dimethylformamide (DMF) is one of a number of 'aprotic polar solvents', which all have the advantage of being able to dissolve a wide range of substances, but do not have the acidic proton that most highly polar solvents have. For many reactions, the acidic proton can lead to	Thank you for your opinion. **Other RMO / Postpone inclusion at least until decision on restriction proposal for NMP (in**

			complications in the reactions. Thus, as industrial solvents they are ideal for certain reaction types. The problem for substitution is that the other aprotic polar solvents with similar physico-chemical properties tend to have the same reproductive hazards. Thus, true substitution for a less hazardous substance cannot be achieved. Currently three of these solvents, Dimethylacetamide (DMAC), N-methylpyrrolidone (NMP) and DMF are being considered for either Authorisation or Restriction. The UK view is that regulatory authorities should aim for a consistent approach to these substances, with coherence under REACH but also between REACH and other legislation, unless there are clear justifications for departing from this principle. In order to avoid regulatory inconsistency and a lack of coherence the UK considers that, in the short term, DMF should not be added to Annex XIV while the Annex XV restriction dossier for NMP is still under consideration by ECHA.	**order to avoid regulatory inconsistency and a lack of coherence)** As acknowledged in your comment, the prioritisation for the inclusion in Annex XIV is based on the criteria set out in Art 58(3) and follows the approach described in the agreed general approach document. In the process of assessing whether a substance on the Candidate List has priority for inclusion in Annex XIV and therefore should be recommended for inclusion in this annex ECHA is not in the position to assess the pertinence of alternative regulatory risk management options for the substance or some of its particular uses. In accordance with REACH Article 59 it is at the discretion of the Member States and the European Commission to decide for which substances Annex XV dossiers with proposals for identification as SVHC are subjected to the SVHC identification process. As you reflect, ideally considerations on the most appropriate RMO should be considered and discussed prior to proposing substances for inclusion to the Candidate List; while the decision to include substances in Annex XIV is taken by the Commission via the regulatory procedure with scrutiny under Article 133(4). While we acknowledge the desire for regulatory consistency, we also recognise the challenges both in defining the scope of such consistency and in achieving such consistency in general, and in particular during the recommendation step of the authorisation process. Consistency may help (i) in increasing efficiency of the regulatory actions, in particular where the differences in the actions could result in an unwanted transfer to (similar) substances without reducing the risks, (ii) to enhance predictability of the authorities actions and (iii) to support achieving a level playing field. The consistency of regulatory actions can however be viewed from multiple angles and achieving

				consistency with one aspect may result in reduced consistency with another aspect. When seeking consistency there is a need to ensure that there is no undue delay in proceeding with regulatory actions and that the burden of proof is not reverted to authorities to make an upfront assessment of the substance and all its possible alternatives / similar substances. **Availability of suitable alternatives** The obligation to apply for authorisation is a incentive to search for and develop suitable alternatives. While in the short term there appear not to be alternatives, the authorisation title of REACH gives a long term incentive to find them and deploy them when these alternatives are technically and economically feasible. The authorisation process foresees that the availability of suitable alternatives for a use of an SVHC are addressed at the application phase of the authorisation process because it is this phase where the respective assessment can be done in an effective matter: based on structured input of information by the applicant; the foreseen dedicated public consultation for scrutinising this information; and the involvement of Committees having the respective expertise and mandate. Information on (lack of) availability of alternatives as well as the research and development efforts done are taken into account. Furthermore on socio-economic benefits of the continued are an important basis for the Socio-economic Analysis committee when it gives its opinion on, for instance, the length of the review period. Naturally the information of the availability (or non-availability) of alternatives is an important element when the final decision by the Commission is taken on whether to grant the authorisation. In addition to the incentive to search for alternatives, documenting this search and having it reviewed, the authorisation requirement also provides an additional level of scrutiny on the control of risk,

				including a possibility to impose further conditions, where needed.
2226	2013/09/17 08:46	Company, Germany		-
2225	2013/09/16 19:33	Company, France		-
2224	2013/09/16 18:53	Industry or trade association, Italy	Actually aren't available valid substitution of DMF for industrial uses. At industrial uses, in our company, DMF is entirely recovered through solvent abatement system for coating PU processes. During production processes many prevention measures are taken such as: - uses of PPE - level controls - medial reports of systematic screening of all operators DMF is handled in closed system that reduce significantly the risk of dispersion in the environment. All processes comply with EU Directi 2009/161/EC and 1999/13 EC as industrial processes. All product that comes from outside EU have no rescriction about DMF as described in REACH.	Thank you for your comment. **No alternative** Please refer to response to comment 2455. **DMF use pattern in specific industrial sectors/companies** Please refer to response to comment 2456.

2223	2013/09/16 15:12	Exopack Advanced Coatings, Company, United Kingdom	Summary EAC has been manufacturing DMF-based films for use in wound dressings for over 20 years. Exposure risks to employees and the general public are already adequately controlled by existing workplace exposure limits and atmospheric emission limits imposed by our LA-IPPC operating permit. The manufacturing process is contained within a single industrial site thereby limiting the potential for exposure to a relatively small number of trained individuals. Exposure of employees is adequately controlled by a combination of engineering, procedural and personal control measures. The risk to the general public is negligible as process emissions to atmosphere are destroyed by thermal oxidation and all waste is removed from site for use as fuel in a controlled industrial process. The site does not discharge any DMF to land or water. There is no risk to intermediate processors, or end users, of the films produced by EAC as the levels of free DMF in the finished products are negligible. The use of DMF is necessary to dissolve the special polymers required to provide the technical product characteristics sought by customers. These have been shown to have significant clinical benefits resulting in improved patient care. The alternative solvents we have found that could possibly be used as replacements for DMF in our solvent systems are other aprotics which have similar reprotoxic hazards as DMF. Process overview EAC manufactures breathable polyurethane films that are used as components of advanced wound dressings for the medical industry. The polyurethane mixes are dissolved in a blend of solvents, one of which is DMF. The films are manufactured by casting the polyurethane mix onto paper or plastic film and drying off the solvents in hot air ovens. Occupational exposure risk management The main processes with potential for operator exposure to DMF are - Delivery and storage of raw material Coatings preparation Coating application under clean room conditions &	Thank you for your comment. **Risk controlled, no alternatives, social-economic benefits of the use** Please refer to response to comment 2455. **DMF use pattern in specific industrial sectors/companies** Please refer to response to comments 2456.

			controlled temperature and humidity Delivery and storage of raw materials DMF, and mixes containing DMF, are delivered to site in steel drums and stored in a purpose-built, chemical warehouse. Drums remain sealed at all times while in the warehouse thereby eliminating any risk of exposure during normal operations. The warehouse is fully bunded and equipped with a fixed foam fire suppression system. DMF and mixes are delivered in closed drums to the coatings preparation area via an enclosed, indoor link. The link is protected by interlocked steel fire doors at each end. Coatings preparation Coating mixes are made by a blending operation under ambient conditions. No external heat or pressure is used. The mixing room is separated from the rest of the factory by steel roller shutter doors. The blending vessels are equipped with exhaust ventilation and the vessels themselves are individually located inside ventilated booths within the mix room. Air extracted from the vessels and booths is abated via two regenerative thermal oxidisers before going to atmosphere. The coating mixes are then pumped to the coating machines through a closed system incorporating pumps and filters. Coatings application Coatings are applied to a continuous web of paper or plastic in a self-contained room at one end of the coating machine. DMF levels in the room are controlled by use of an enclosed feed system and by extraction at the point where liquid coating is applied to the moving web. Further operator protection is provided by the use of PPE such as filter masks, eye protection, chemical barrier gloves, coveralls, etc. and by minimising the time operators spend in this room. Control of the coating process is done from a separate room equipped with continuous VOC monitoring instrumentation (PID). The readings from the PID are backed up by DMF detector tube measurements taken each shift. All results are recorded and reviewed daily by the H&S department prior to the daily operations meeting. Both rooms of the coating machine are maintained under	

			cleanroom disciplines. The upper plant rooms housing the dryers are equipped with "DMF in Use" warnings that automatically illuminate at each entrance. Periodic analysis of DMF metabolite in post-shift urine samples is used to check the effectiveness of the control measures. The results of urine testing give an estimate of the total exposure by all routes (mainly inhalation and skin contact) and are evaluated against internationally recognised biological monitoring guidance values. The company's incident reporting procedure requires any instances of above normal atmospheric levels to be reported and investigated. Any instances of alcohol induced flushing, indicative of DMF exposure, also have to be reported. The Company requires all spills of hazardous substances greater than 5 litres to be reported, investigated and acted upon. General measures DMF was identified as a Substance of Very High Concern (SVHC) because it carries the R61 Risk Phrase " May cause harm to the unborn child ". This risk can be completely avoided by taking appropriate steps to ensure pregnant women are not exposed to DMF. EAC's policy is to inform successful female job applicants in writing about the risks associated with DMF at the point of making a job offer. The new employee is advised that she must inform the company as soon as possible if she is trying to start a family so that any risks associated with her job can be reviewed and steps taken to ensure her safety. Risk to general public / local environment EAC's UK operations are permitted and regulated as an LA-IPPC Part A2 installation under the Pollution Prevention and Control regulations 2000. The Permit is issued and regulated by the Local Authority to ensure Best Available Techniques are used to control emissions to all media - i.e. air, land and water courses. EAC is also regulated for water and land pollution by the Environment Agency under a River Dee Water Protection Zone Consent. Process emissions from all solvent dispensing areas, mixing vessels, mixing booths and coating machines are abated via two regenerative thermal oxidisers before	

			going to atmosphere. An emission limit for DMF of 2 mg/m3 is imposed under the site's operating permit and compliance with this condition is monitored by an external company. EAC also has in-house capability to monitor total VOC emissions using Flame Ionisation Detection (FID). The FID readings are displayed in the Shift Supervisors' and EHS Manager's offices at all times. The FID system is also set to alarm machine operators if emissions exceed pre-set values and automatically instructs operators to shut down the machines. The atmospheric emission limit imposed by the Permit (2mg/m3) is well below the 8hr TWA Workplace Exposure Limit for DMF of 15 mg/m3. EAC does not discharge any process waste to drains. All wastes containing DMF are removed from site by an authorised waste contractor and are used as secondary fuel in an industrial process. The risks of pollution to the land or water courses are therefore very low and are well controlled. Consumer Exposure All EAC medical products manufactured using DMF are cast polyurethane films which are dried to a controlled level of retained solvent. Product specifications and testing methods are designed to ensure levels of DMF in the finished films are maintained below 0.1%. In practice retained solvent levels in films leaving EAC are typically around 0.03%. All films are subject to further processing by EAC's customers and DMF levels in products reaching the general public are much lower still. This has been demonstrated by solvent retention tests on fully processed and sterilised customer samples. EAC's quality control systems are routinely audited as part of the company's ISO9000 accreditation and in addition, supplier quality audits are carried out by medical customers. It is normal for medical customers to include a requirement in their specifications that all quality records are available for inspection so external audits can occur at any time. All EAC products made using DMF are destined for medical use and as such are subject to further regulatory control, according to ISO 10993, whereby medical products are tested for cytotoxicity, skin irritation and skin sensitisation. Alternative technologies	

			EAC have considered alternative technologies over many years primarily to reduce the DMF exposure risk to employees. Technologies investigated have included: - alternative solvents - water-based systems - extruded films A programme of work was initiated in 2003 to try to eliminate the use of DMF as a solvent. The Company contacted a number of suppliers of polyurethane resins with a view to identifying an alternative in a safer solvent blend. A number of potential alternatives were identified and evaluated but were found to be unsuitable. The alternatives evaluated to date have not provided a polymer system with functional performance similar to the resin system currently used. In particular, we have been unable to obtain a film that has similar tensile and elongation properties in both the dry and wet state. These are key functional parameters of the polyurethane film and determine the ability to meet end users' requirements in a medical product. There are a limited number of polar solvents capable of dissolving high molecular weight polyurethane resins. Alternative solvents such as DMAc and NMP are capable of acting as alternative solvents for the current polyurethane type but have similar toxicological hazards as DMF. Socio-economic impact The polyurethane films produced by EAC are sold to many well known global medical companies for use as the support layer for wound dressings. Over 90% of the material sold is utilised in dressings that are used in a hospital environment, mostly for the treatment of chronic conditions in the elderly, where infection control is of paramount importance. The materials produced by EAC provide a bacterial barrier and therefore help to control infection. Other materials could provide a bacterial barrier but the DMF based polyurethanes are breathable, bringing two significant advantages 1) Clinically proven advantages versus non bacterial barrier and non breathable systems. Many papers have been written showing the advantages of advanced woundcare products over “traditional” dressings. 2) Lower overall cost in relation to traditional	

			dressings. One of the key advantages of breathable polyurethanes coated by EAC is that the dressings made utilising these materials can stay in place, without the need for nursing intervention, for four days or more. Although a traditional dressing is less expensive than one based on a DMF-based polyurethane, nursing intervention (dressing changes) are required every day. Reducing nursing intervention has the further advantage that the opportunity for infection of the wound during dressing changes is minimised.	
2214	2013/09/13 16:25	Company United Kingdom	We understand why DMF has been classified as a CMR and consequently why it has become an SVHC. However we do not understand or accept the logic which is suggesting Prioritisation for Authorisation. We recognise that the purpose of REACH legislation is to protect workers and members of the public but we believe the industrial use of DMF is already well controlled under existing regulatory regimes. Firstly, in England, the COSHH regulations enforced by the Health and Safety Executive gives a legal requirement that all operations should adhere to the WELs of 5ppm for an 8 hr. average and 10ppm for a 15 min peak exposure. This is in line with the European	Thank you for your comment. **Prioritisation logic** Please refer to response to comment 2488. **Risk controlled** Please refer to responses to comments 2456.

			Commission's third directive on Occupational Exposure Limits 2009/161/EU. We have an active programme of monitoring our workers total exposure via end of shift urine tests to quantify DMF metabolites, specifically n-methylformamide (NMF). This has the added benefit that it would also highlight any potential skin contact that may have occurred. Since 1996 we have carried out 11,941 urine tests and only 43 have indicated a breach of the exposure limit, these have all been investigated and improvements made. Secondly, the Environmental Permitting (England and Wales) Regulations 2010 enforced by the Environment Agency specify a range of measures for protecting the environment including Emission Limit Values for vents which we are required to comply with, measure and report. These regulations implement parts of many community directives in particular Directive 2008/1/EC concerning integrated pollution prevention and control. Any industrial users of DMF will also be covered by these regulations and as a consequence the risk to workers and the environment will be controlled and minimal. We are not aware of any use other than industrial and hence controlled. Exposure of the general public through traces of DMF left in products is also prevented by the measurement and control of processes during manufacture. This results in levels far below the 1000ppm specified under the REACH legislation and indeed can be below detection limits. Consequently we believe that inclusion into Annex XIV and Authorisation will not result in any added safety benefits for workers, environment or the public. It will however lead to significant costs and difficulties for SMEs and could compromise the viability of European manufacturers. This will result in giving an unfair competitive advantage to Asian manufacturers who are not constrained by Authorisation. Also without the internal control of European manufacturers the potential for high levels of DMF retained in the product will increase. The net effect of this will be an increase of risk for European consumers.	
2205	2013/09/11 08:22	Company Germany	N,N-dimethylformamide (DMF) is used in our company for manufacturing (synthesis) and purification of electronic chemicals. We have to prepare products with a purity of at least 99,5%. Accordingly purification	Thank you for your comment.

			procedures are one of the key steps to get the chemicals in the required quality. Technical alternatives are not yet available to replace DMF. All research for alternative solvents or technologies has not led to adequate results. Other similar polar, aprotic solvents like NMP, formamide, N,N-dimethylacetamide or DMSO result in final products with insufficient performance. Additionally most of the tested alternatives have the same intrinsic properties or are on the Candidate List too. Therefore substitution of DMF as solvent in chemical synthesis and purification of our main products is currently not possible. The use of N,N-dimethylformamide in our company is an industrial process, managed by high skilled operators. The synthesis is done either in closed , continuous process with occasional controlled exposure (PROC 2)or in closed batch processes (PROC 3). Process measures (e.g. local exhaustion) are implemented in order to control workplace exposure. So there is an appropriate control of residual risks. Measurement data are available which show that the measured exposure is only 10% of workplace exposure limit (WEL). DMF is neither part of formulations nor part of articles or products. The inability to use DMF or introduction of less hazardous alternatives in the manufacturing and purification process of the fine chemicals used in the electronic industry will adversely impact the production of our main product. So we expect negative impacts on the economic situation and on long term security of workplaces in our company.	**No alternative** Please refer to response to comment 2455. **DMF use pattern in specific industrial sectors/companies** Please refer to response to comment 2456. **Plant closure, competitive disadvantage, socio-economic impacts** Please refer to response to comments 2415, 2488 and 2455.
2199	2013/09/10 12:50	Company United Kingdom	REACH Annex XIV – Authorisation Comments on the 5th Draft Recommendation of Substances for Inclusion in Annex XIV – DMF (N,N-dimethylformamide CAS No. 68-12-2) We are a UK company operating within the industrial sector operating a unique process manufacturing high performance textiles. We are subject to a Local Authority Pollution Prevention Control (LAPPC) Operating Permit involving VOC emission abatement in accordance with the requirements of the primary legislation, the Solvents Directive	Thank you for your comment. **Consistent approach with similar solvents, other RMO, imported articles** Please refer to response to comment 2427. **Risk controlled** Please refer to response to comment 2455. **Exemption**

			1999/13/EC. Our process, which falls under Process Category PROC 5 (Mixing or blending in batch processes (multistage and/or significant contact)), involves both mixing and coating operations. These take place in fully 'closed' systems, incorporating solvent capture, where we operate appropriate control measures to minimise exposure to humans and the environment. As has been acknowledged in ECHA's Draft Background Document for DMF (dated 24 June 2013), we, as an industrial user, fully employ management measures in order to control both workplace and environmental exposure and occupational controls (occupational exposure limits (OEL) are monitored and recorded) are carried out in addition to personalised training and formalised audited system procedures. We are aware that different aprotic solvents are currently being treated differently under REACH - NMP is under consideration for Restriction whilst others, such as DMF and DMAc, are proposed for Authorisation. It is our belief that the toxicological properties for this solvent group are comparable which leads us to recommend that they should all be treated in a similar way for the purposes of REACH. As a company, we are already investing to develop alternative technologies for our coating systems but since our customers' approval processes for our type of products take 4 to 6 years to complete, an alternative system could take up to 10 years to implement fully. We have also invested over 1 Million Euros by upgrading our exposure control regimes for both worker and environmental protection and believe that these initiatives demonstrate that we are taking a fully holistic approach to both our short and long term responsibilities. As a member of the UK coatings industry Working Group we would urge that a Restriction approach for DMF be considered as a serious alternative to Authorisation, with restrictions put in place for use in open systems where it is such operations that pose the greatest risk of exposure to man and the environment. We believe that such a Restriction would deliver comparable minimised exposure with the added benefit of reducing the burden for both the authorities and industry that Authorisation	Please see response to comment 2278

			would impose. We also believe that in the longer term, Authorisation would significantly impact on the manufacturing capability of manufacturers who currently use DMF and this would open the door to significant non-EU import penetration into the EU of articles giving rise to a possible risk of higher DMF exposure levels to the population. Alternatively, we would support an exemption for fully 'closed' system operations, where all relevant regulatory constraints are met (OEL's, emission standards etc, etc) should Authorisation be the route ultimately followed by the REACH process. 10 September 2013	
2198	2013/09/09 15:32	International organisation United Kingdom	When used as an industrial solvent the solvent is removed at the end of the process and as such any risk to human health and the environment is minimal. Is is believed that existing community legislation and QHSSE recommendations to protect human health are in place in regards to DMF for use as an industrial process solvent eg. occupational exposure limits in Commission Directive 2009/161/EU. Additional local QHSSE regulations such as risk assessments and UK COSHH ensure safe working conditions.	Thank you for your comment. **Exemption** Please refer to response to comment 2456. **Risk controlled, no suitable alternative** Please refer to response to comment 2455.
2194	2013/09/05 17:10	Company Netherlands	We think the inclusion of DMF in the ANNEX XIV list is not favorable because DMF is an important chemical used as a polymer solvent in the synthetic leather industry. Especially the wet production process of breathable synthetic leather. The use of DMF in this production process is relative safe and there is no good alternative for DMF in this process for DMF. The authorization of this product will force us to relocate our production to outside the EU and this will cost in our specific case the loss of 50 jobs directly and approx another 100 jobs indirectly in Europe.	Thank you for your comment. **No alternative** Please refer to response to comment 2455. **Relocation outside EU** Please refer to response to comment 2415.
2193	2013/09/05 14:44	PENNEL & FLIPO Industry or trade association Belgium	nous n'avons pas d'alternative pour la transformation des enductions TPU	Thank you for your comment. **No suitable alternatives** 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. 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.
2170	2013/08/28 12:56	Company United Kingdom	Uses:- We are a U.K.company operating within the industrial sector of coated technical woven textiles. The predominantly organic solvent based industrial chemical coating processes undertaken on our site are subject to a Local Authority Pollution Prevention Control (LAPPC) Operating Permit involving VOC process emissions abatement in accordance with the requirements of the primary legislation, the Solvent Emissions Directive 1999/13/EC. According to ECHA's dissemination database of registered subsatnces, our process falls within Category PROC 5, although broadly speaking it can be described as a 'closed'	Thank you for your comment. **No alternatives, risk controlled** Please refer to response to comment 2455. **Consistent approach with similar solvent, other RMO, imported articles** Please refer to response to comment 2427. **Competitive disadvantage** Please refer to response to comment 2488.

			system incorporating appropriate control measures to minimise exposure levels. A significant proportion of our coated fabric output requires the use of formulated coating solutions whihc utilise DMF (N,N-dimethylformamide, CAS No. 68-12-2). For our products and processes, there is presently no viable alternative nor any immediate prospect of a viable alternative for DMF. However, and particularly since it is a requirement of the Operating Permit, in conjunction with our raw material suppliers the search for an acceptable alternative substance is ongoing. It is noted that substances previously proposed as alternatives have a similar hazard profile to DMF, but for our particular application, with the current polymers involved, these are most definitely not useful options either in terms of processability or solvent power. Importantly, in the Draft Background Document for DMF dated 24.06.2013, it is also noted that the majority of uses are in inductrial settings and that there is no registered use for consumers. Releases:- The classification of DMF as a Category 1B reprotoxic substance has resulted in its designation as an SVHC (Substance of Very High Concern), and subsequently to prioritisation for Annex XIV Authorisation. In the Background Document the specific risk (Intrinsic Properties) is stated as "May damage the unborn child" and gives this as the reason for its inclusion on the Candidate List for Authorisation on the 19th December 2012. Firstly, in terms of an industrial environment operating under 'closed' system environmental controls, it is claimed, in terms of Occupational Exposure Limits, that high concentration levels of DMF do not occur and that secondly, as part of the Risk Management procedures pregnant women are not permitted to be exposed to such environments. Consequently there is no real opportunity for harmful exposure to occur through direct skin contact or inhalation. In our case captive VOC emissions abatement is by means of an RTO (Regenerative Thermal Oxidiser) and consequently DMF is confined to the process system and does not represent a direct external exposure risk to human health or the environment. Furthermore, as we have previously stated, it is our understanding, as a	

			member of the UK DMF Working Group, that only industrial users are actually registered and that there is no registered use for what are termed 'consumers'. As you have acknowledged, within the industrial setting, Occupational Risk Management is controlled through system wide operations such as VOC abatement of captive emissions, including Local Exhaust and Ventilation (LEV) installations, supplemented by appropriate PPE (Personal Protective Equipment), personnel training and formalised audited systems procedures. Occupational Exposure Limits (OEL) are monitored and recorded. We have noted that the different aprotic solvents are traeted differently under REACH; for example NMP is under consideration for Restrictions procedure whilst others, such as DMF and DMAc are proposed for Authorisation. In view of the fact that we are informed that they all have comparable toxicological profiles it seems logical to us that they should all be treated in the same way. As part of the UK coating industry Working Group we have previously advocated the 'suitability of Restrictionfrom open systems as the appropriate control method for DMF. Authorisation we understand would be excessively costly, particularly so relative to the smaller companies, with an excessively bureaucratic workload on all involved in its application and administration; in the longer term it has been argued that it could lead to a significant non-EU import penetration into the EU resulting in a loss of EU employment and possibly an increase in the risk of higher DMF exposure levels to the population.	
2165	2013/08/27 18:39	Company United Kingdom	We do not recommend the inclusion of DMF in Annex XIV as we feel that the occupational exposure limits for the substance are an appropriate alternative method of control. Such limits form part of the Restriction Dossier for NMP.	Thank you for your comment. **Risks controlled** Please refer to response to comments 2456 and 2455. **Other RM/ consistent approach with similar solvents** Please refer to response to comment 2427.
2161	2013/08/21	AGTC Bioproducts Ltd	DIMETHYLFORMAMIDE CAS 68-12-2 EC 200-679-5, SVHC	

	17:02	Company United Kingdom	list This material is used extensively in the synthesis of peptides for use in basic research. It is invariably handled in a controlled environment (synthetic laboratories are very used to handling dangerous materials) and as far as we can see reprents a very low hazard to the people working directly with the material. The synthesis is carried out in a sealed environemt, the waste is collected and stored in sealed containers and disposed of in the authorised and approved manor as required by the institute in which the laboratory is located. In our view this material does not present a significant risk to the operatives and the and the end products of their work contribute significantly to the overall well being of the human race.	Thank you for your comment and the information provided on your specific application in synthesis of peptides fur use in basic research. Note that 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). 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. As regards the use of DMF in synthesis of peptides fur use in basic research, this may fall under the exemption of the use of substances in scientific research and development from the authorisation requirement in accordance with Art. 56(3). We would suggest that you examine whether the mentioned use of your substance can be regarded as SRD in accordance with the definition set out in Article 3(23). Article 3(23) defines SRD as "any scientific experimentation, analysis or chemical research carried out under controlled conditions in a volume less than 1 tonne per year". If you conclude that your use of DMF fulfil the above points, that use can benefit from the exemption of SRD from authorisation as set out in Article 56(3) and no authorisation would be required to continue the use after the sunset date.

				It appears that only substances used directly for research (or analytical purpose), whether on their own, in mixture, or in conjunction with analytical equipments, can benefit from the SRD exemption.
2157	2013/08/21 11:56	European Trade Union Confederation Trade union Belgium	ETUC supports the recommendation to include DMF in the REACH authorisation list. DMF is included in the Trade Union Priority List for REACH authorisation: http://www.etuc.org/a/6023	Thank you for the information, and for providing your opinion.
2152	2013/08/19 09:59	European Industrial Gases Association (EIGA) Industry or trade association Belgium	On the scoring: EIGA notes that DMF having scored 18 out of a possible 27, has been prioritised as at least sixth (now fifth as one other substance has been removed from the 2013 priority list) out of one hundred and forty four substances on the candidates list. EIGA challenges the scoring that has justified this prioritisation. • DMF has scored 0 (lowest possible) in terms of its inherently hazardous properties This appears corrects as DMF is not a PBT or vPvB substance. DMF qualifies to be considered for SVHC only on the basis of "hazard to the unborn child" (H360D). • DMF quantity used in Europe is stated as 100,000 to 120,000 tonnes per year and scored as 9 i.e. highest available score. EIGA cannot comment on the total usage in Europe, this should be data sourced from the manufacturers. • DMF exposure routes has been scored as 3x3=9 i.e. highest available score. EIGA cannot comment on the 3 for "Uses in industrial settings at a high number of sites". EIGA does challenge the 3 for "Significant potential for worker exposure from uses within the scope of authorisation" on the basis that all of the uses described in the prioritisation document are industrial and indirect contact i.e. closed processes EIGA's experience is that worker exposure is a lot less than as described in the prioritisation document, where it says exposure is >4hrs/day and <240 days per year (see Attachment in Section 4) On this basis a scoring factor of 0 or 1 is the correct worker exposure value. That would make the exposure route score 0 or 3, instead of 9.	Thank you for your comment and the information provided. **Exemption request** With regards your request to exempt from the authorisation process the use of DMF as solvent and stabilizer for acetylene in bundles of gas cylinders, in multiple elements gas containers (MEGC) and in battery-vehicles ECHA stresses that according to Article 58(2) REACH it is possible to exempt from the authorisation requirement uses or categories of uses '(…) provided that, *on the basis of the existing specific Community legislation imposing minimum requirements* relating to the protection of human health or the environment for the use of the substance, the risk is properly controlled'. This basis has not been provided here. As DMF 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. Please refer to response to comments #2456 for further information on the elements considered by ECHA when deciding whether to include an exemption of a use of a substance in its recommendation. **WDU score** Note that the prioritisation for the inclusion in Annex XIV is based on the criteria set out in Art

			This would make the total score 9 or 12 instead of 18. That will reduce the priority placed upon DMF in the selection from the candidates list	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). 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). Further details on the priority of DMF (according to Art 58(3) criteria) is provided in the response to comment 2488. The use and user specific conditions can be reflected in the authorisation application and they will be taken into account by 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. **Volumes reported in the background document** In addition, please note that the DMF draft background document doesn't refer to DMF quantity used in Europe as being 100,000-120,000 tonnes per year, nor does it provide information on frequency and duration of exposure (>4hrs/day and <240 days per year), as indicated in your comment. The draft background document states that the amount of DMF manufactured and/or imported into the EU is, according to registration data, in the range of 10,000 – 100,000 t/y.
2099	2013/06/25 10:35	Individual France	no comments	-

II - Transitional arrangements. Comments on the proposed dates:

#	Date	Submitted by (name, Organisation/MSCA)	Comment	Response
2473	2013/09/23 19:31	ChemSec, International NGO, Sweden	It is assumed that the Commission Regulation including the substances of this 5th Recommendation in Annex XIV would enter into force only in February 2015. Keeping the proposed application date would mean an application date by August 2016 with an extra 18 months to sunset the substance. There is no reason why the date for inclusion in Annex XIV for this substance should be so far ahead leading in a delay for the realisation of effective protection objectives i.e. February 2018. Potential applicants are already informed of the likely inclusion of the substance in Annex XIV or will be when a decision on inclusion in Annex XIV is taken. A 2 years preparation period for application submissions should be more than sufficient to prepare for applications. According to REACH (Art 58.1 ii) a minimum 18 months period is only foreseen between the sunset date and the application deadline, but nothing prevents ECHA / the European Commission to foresee an earlier deadline for application. Therefore ChemSec would propose to provide for an effective deadline for application of maximum 2 years from the date of the EU Commission's decision to include the substance in Annex XIV.	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.
2455	2013/09/23 17:38	European Diagnostic Manufacturers Association	EDMA does not support Authorisation as the most appropriate risk management option for the reasons mentioned under the	Thank you for your comment.

		(EDMA), Industry or trade association, Belgium	'General Comments' section. If the EU should regardless decide to proceed with including DMF on REACH Annex XIV, the IVD sector would require a 7-10 years' transition time considering the hundreds of products which would be impacted, the majority SME nature of our sector, and the extensive re-validation and re-registration required both in the EU and internationally. IVD manufacturing is impacted during this same timeline by the proposed prioritisation of 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-OPnEO) which, if listed on Annex XIV, would considerably increase the complexity and time needed to address identification of substitutes and redesign products. In some cases, both (sets of) substances are included in the manufacture or formulation of the finished IVD products. EDMA therefore requests longer transitional arrangements on the basis that the IVD sector might need to apply for Authorisation for two or more substances critical to the sensitivity and specificity of our diagnostic tests. It is not feasible for one industry to plan for the substitution of multiple different substances that are used in IVDs on the basis that global supply of these devices must be maintained and validation processes are estimated to take up to 10 years for a single substitution. Should both (sets of) substances be listed on Annex XIV, the IVD industry would potentially need much longer than 10 years to test for candidates and engage in re-validation/registration processes.	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. 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 are no viable reasons for adjourning the subjection of a substance or some of its uses to authorisation. Information regarding lack of alternatives is however important information for inclusion in an authorisation application. This information will be taken into account by the Risk Assessment and Socio-Economic Analysis Committees when forming their opinions and by the Commission when taking the final decision. It may impact the decision on granting the applied for authorisation and the conditions applicable to the authorisation, such as e.g. the length of the time limited review period of the authorisation. Regarding the time needed to prepare potentially multiple/parallel applications (for DMF and 4-tert-OPEO), please note that in accordance with Art. 62(1, 2)

				applications for authorisation may be made by the manufacturer(s), importer(s) and/or downstream users of a substance (or any combination thereof) and that they may be made for one or several uses. Applications may be made for the applicant's own uses and/or for uses for which he intends to place the substance on the market. From these specifications of Art. 62 it is evident that not each actor on the market has to apply for authorisation of his use(s). A supplier (manufacturer, importer or downstream user) may cover in his application use(s) of his downstream users. Furthermore, it is possible to submit joint applications by a group of actors. To get the required application(s) ready in time is therefore also a matter of communication, organisation and agreement between the relevant actors in the supply chain and efficient allocation of work. Following the General approach for preparation of draft Annex XIV entries for substances to be included in Annex XIV, ECHA has used 18 months from the inclusion of the substance into Annex XIV as the standard latest application date (LAD) and then spread the latest application into 6 months (3 lots), mainly to account for the anticipated workload of the Agency with regard to processing of authorisation applications. In this context, DMF has been assigned to the first lot (recommended LAD of 18 months after inclusion to Annex XIV) in order to reduce the potential transient evasion of the authorisation requirement

				for another substance already recommended for inclusion in Annex XIV, which has similar inherent properties and uses with DMF (N,N-dimethylacetamide; DMAC).
2449	2013/09/23 17:05	Company, Germany	We do not support authorisation as the most appropriate RMO for DMF for the reasons mentioned in the attached EDMA paper. if DMF should nevertheless be included in Annex XIV then a transition period of 7 to 10 years is required given the hundreds of products/assays that will be affected and the absence of any suitable alternative. Re-validation and re-registration both in the EU and internationally will also be required.	Thank you for your comment. Please refer to response to comment 2455 in this section.
2448	2013/09/23 17:02	Vetex n.v., Company, Belgium	In case the use of DMF in the textile coating would not be exempted from authorization, the transitional period should be as long as possible; minimum 12 years.	Thank you for providing your opinion.
2441	2013/09/23 16:23	DINOX Handels-GmbH, Company, Germany	Seeing most the partially very detailed comments from users and the reaction of ECHA to this comments, it does not give us the impression that anything is going to stop this process.	Thank you for providing your opinion. Please see response to your comment in section I. Regarding the process, note also that the draft Annex XIV entries for priority substances recommended for inclusion in Annex XIV will be discussed in the Member State Committee who will issue an opinion (Art.58(3)). The Agency shall update its draft Annex XIV entry for substances recommended for inclusion in Annex XIV taking into account the comments and then send this recommendation, after consultation of the Member State Committee, to the Commission. The final decision to include substances in Annex XIV is taken by the Commission via the regulatory procedure with scrutiny under Article 133(4). It should be noted that the Commission is not bound by the prioritisation given in the Agency's

				recommendation.
2434	2013/09/23 15:51	EFPIA, Industry or trade association, Belgium	No Comment	-
2431	2013/09/23 15:37	GIFAS, Industry or trade association, France	Please refer to attached document	Thank you for your comment. Please refer to response to comment 2455 in this section.
2423	2013/09/23 15:01	Company, Czech Republic	All the medicinal product undergou GMP rules for production and manufacturing procedure are subject to authorization state institutions for drug medicines control . Authorisation procedure includes an assessment of a dossier in which is assesed safety, efficacy, and quality of the product of course indications and contraindications. Any change in registration is subjet to research and development and approval of above mantioned authorities in all countries where is final product maketed. DMF is used as solvents during manufacturing intermediates and final products and is not present in thems.	Thank you for your comment. Please refer to response to comment 2455 in this section. (Please also refer to the answer to comment 2423 in section I)
2415	2013/09/23 14:02	Individual, Italy	Endura's investigation has highlighted that a concrete alternative to DMF to be used as a solvent does not exist. The research activities carried out until now in the laboratories, with the aim to substitute DMF with another, safer solvent than DMF, has not led to a tangible result. Therefore Enudra believes that it will be impossible to find an alternative to DMF by the predictable sunset date that should be in February 2018. Especially as, if an alternative solvent eventually will be identified, it will require time to find and develop (if at all possible) all relevant related plant and facility modifications. Endura's current industrial plant is not prepared for the use of different solvent than DMF, and significant time and investments would be necessary to adapt them. Moreover, to change the solvent could impact the regulatory dossiers (Biocidal, REACH and Pharmaceutical uses) connected to it. For example, in the case of the synthesis of the intermediates, if the plant is modified, the strictly controlled conditions described in the correspondent REACH registration dossier must be updated. The impact on the registration dossiers could be even higher if we refer to the Biocidal Regulation or to the pharmaceutical uses. For example, in the case of pharmaceutical used, if the hypothetic new solvent adopted will be present, even if only in traces, in the final product, the quality dossier will have to be amended, the safety of the drug should be reconsidered and a re-approval should be required by the competent authorities. A similar situation could occur for	Thank you for your comment. Please refer to response to comment 2455 in this section.

			biocidal uses.	
2414	2013/09/23 13:38	Company, Germany	Abbott strongly opposes the inclusion of DMF onto Annex XIV and asks ECHA to consider more appropriate risk management options in the context with the whole group of other polar aprotic substances (as outlined in the general comments), due to the criticality of the use in the IVD industry. However, if ECHA decides to proceed towards authorization, Abbott requests ECHA to consider longer transitional arrangements on the basis that substitution of DMF is a complex, time consuming process subject to approval by many regulatory agencies worldwide. In order to replace key substances used in manufacturing of IVD tests or as test constituent, extensive studies would be required to screen candidate replacements to ensure no change in product performance – in particular sensitivity and specificity testing. This may include testing of large populations of patients, in order to make sure that rare variations in the blood proteins of some patients wouldn't interfere with the safe diagnostic performance of the test, leading to potentially fatal consequences for an individual patient. e.g., in a HIV test. Additionally, full stability trials on 3 lots of the reformulated component would be necessary to introduce such a change. Any change such as this would mean relicensing in certain markets, leading to protracted introduction time and a complex implementation pathway for the products. The validation testing studies– and re-registration would need to be done on an individual product-by-product basis. Because the test constituents produced using DMF can be used in several different final products (IVD test kits) other tests which run on the same large automated analysers in a hospital or blood bank can be impacted also. That means, a replacement process could impact entire portfolios of diagnostic tests on this analyser, i.e. all the different blood parameters or disease markers. The time to implement such a portfolio redesign would be considerable. The complexity of substitution, the resources needed and the costs incurred could cause companies to evaluate whether to remove some products from the market and/ or to relocate manufacturing outside the EU. Furthermore, IVD manufacturing is likely to be impacted to some extent during this same timeline by the proposed prioritisation of 4-tert- OPnEO which increases the complexity and time needed to address identification of substitutes. In some cases, both DMF and 4-tert OPnEO are included in the	Thank you for your comment. Please refer to response to comment 2455 in this section.

			manufacture or formulation of the finished IVD products. Abbott therefore requests longer transitional arrangements on the basis that the medical devices sector is potentially impacted by EU activity on these substances and as well as proposed activity on other aprotic polar solvents. In addition, should authorisation be required, multiple, parallel applications could be necessary. It is not feasible for one company to plan for the substitution for multiple substances that are used in IVDs on the basis that global supply of these devices must be maintained and validation processes are estimated to take up to 10 years (see attached table on confidential attachments).	
2356	2013/09/20 20:21	Company, France	We didn't find any proposition of application and sunset dates in the background document.	Thank you for your comment. The suggested timelines are included in the draft entries to be inserted in Annex XIV (this document is available under "Related documents", as explained in the public consultation website). The proposed latest application date for DMF is "Date of inclusion in Annex XIV plus 18 months" and the sunset date as "Latest application date plus 18 months."
2347	2013/09/20 18:27	Company, Ireland	N/A	-
2343	2013/09/20 17:33	Individual, Italy	The chemical-physical properties of DMF make it currently irreplaceable for many industrial applications (solvent producing polyurethane, intermediates and medical products, synthetic and artificial leather, fibres, intermediates and solvent for acetylene). Nevertheless for several years it has been going on an important commitment to identify a valid substitute of DMF for industrial usages. Unfortunately at the moment a solution has not been found. Therefore, it's impossible to expect that European industries will have identified an alternative choice to DMF by February 2018 (the predicted sunset date). It is thus necessary to ensure to European industries the necessary time to find and develop (if at all possible) a substitute to DMF, as well as to leave them the time required to change all the industrial facilities. In fact the current industrial plants are not suitable for processes which use a different substance than DMF, and a long time would be necessary to adapt them, as well as huge investment. For example, for the	Thank you for your comment. Please refer to response to comment 2455 in this section.

			use of DMF as solvent for acetylene, it would be necessary to change all cylinders in acetylene, that have a typical lifetime of 50 or more years, and that would have to be scrapped prematurely. The total population of acetylene cylinders in DMF service in Europe is estimated at more than 150 000. While for the production of synthetic and artificial leather, synthetic fibres, it would be necessary to change all the existing plants that strictly fit to the use of such a solvent, it would be necessary to change all the DMF recovery systems (such as distillation columns under vacuum). In addition, substitution may require adjustments of the pharmaceutical regulatory dossiers of the medicinal products resulting from the synthesis processes in which the solvents concerned are used. Replacement of a solvent optimised for process reactions, yield and product purity, and controlled for workplace and environmental safety, can have the potential to substantially affect the impurity profile of the final drug substance or even the ability to successfully produce the drug substance. If a new solvent residue is present in a final drug substance, or if the impurity profile of the final drug substance is changed, the safety of the drug substance has to be re-established and approved by the EMA (European Medicines Agency). In addition, it has to be considered that DMF has many different uses and it could be, as a chemical, subjected to different legislations. Some of these required authorization/registration processes with the submission of the chemical dossiers to the Competent Authority. In these dossiers it was described the manufacturing process. If there will be a change in the manufacturing process, or DMF will be replaced by another substance, industries will have to review the dossier and in some cases the Competent Authority will have to evaluate and authorize again it. This happens for example with the biocidal products, and in a similar way with medicinal products.	
2341	2013/09/20 17:24	C.O.I.M. S.p.A., Company, Italy	We agree with the position explained by Federchimica (Italian CChemical Association)	Thank you for your comment. Please refer to response to comment 2455 in this section.
2316	2013/09/20 13:35	Company, Italy	The chemical-physical properties of DMF make it currently irreplaceable for many industrial applications (solvent producing polyurethane, intermediates and medical products, synthetic and artificial leather, fibres, intermediates and solvent for acetylene). Nevertheless for several years it has been going on	Thank you for your comment. Please refer to response to comment 2455 in this section.

			an important commitment to identify a valid substitute of DMF for industrial usages. Unfortunately at the moment a solution has not been found. Therefore, it's impossible to expect that European industries will have identified an alternative choice to DMF by February 2018 (the predicted sunset date). It is thus necessary to ensure to European industries the necessary time to find and develop (if at all possible) a substitute to DMF, as well as to leave them the time required to change all the industrial facilities. In fact the current industrial plants are not suitable for processes which use a different substance than DMF, and a long time would be necessary to adapt them, as well as huge investment. For example, for the use of DMF as solvent for acetylene, it would be necessary to change all cylinders in acetylene, that have a typical lifetime of 50 or more years, and that would have to be scrapped prematurely. The total population of acetylene cylinders in DMF service in Europe is estimated at more than 150 000. While for the production of synthetic and artificial leather, synthetic fibres, it would be necessary to change all the existing plants that strictly fit to the use of such a solvent, it would be necessary to change all the DMF recovery systems (such as distillation columns under vacuum). In addition, substitution may require adjustments of the pharmaceutical regulatory dossiers of the medicinal products resulting from the synthesis processes in which the solvents concerned are used. Replacement of a solvent optimised for process reactions, yield and product purity, and controlled for workplace and environmental safety, can have the potential to substantially affect the impurity profile of the final drug substance or even the ability to successfully produce the drug substance. If a new solvent residue is present in a final drug substance, or if the impurity profile of the final drug substance is changed, the safety of the drug substance has to be re-established and approved by the EMA (European Medicines Agency). In addition, it has to be considered that DMF has many different uses and it could be, as a chemical, subjected to different legislations. Some of these required authorization/registration processes with the submission of the chemical dossiers to the Competent Authority. In these dossiers it was described the manufacturing process. If there will be a change in the manufacturing process, or DMF will be replaced by another substance, industries will have to review the dossier and in some cases the Competent Authority	

			will have to evaluate and authorize again it. This happens for example with the biocidal products, and in a similar way with medicinal products.	
2312	2013/09/20 12:57	CHINOIN Private Co. Ltd., Company, Hungary	No Comment	-
2307	2013/09/20 12:13	SABIC Petrochemical s B.V., Industry or trade association, Netherlands	No comments, as SABIC proposes not to use the authorisation route as Risk Management tool.	Please refer to response to your comments in other sections.
2298	2013/09/20 11:06	Assogastecnici/Federchimica, Industry or trade association, Italy	Assogastecnici has no comments about the dates.	-
2295	2013/09/20 10:40	Federchimica, Industry or trade association, Italy	The chemical-physical properties of DMF make it currently irreplaceable for many industrial applications (solvent producing polyurethane, intermediates and medical products, synthetic and artificial leather, fibres, intermediates and solvent for acetylene). Nevertheless for several years it has been going on an important commitment to identify a valid substitute of DMF for industrial usages. Unfortunately at the moment a solution has not been found. Therefore, it's impossible to expect that European industries will have identified an alternative choice to DMF by February 2018 (the predicted sunset date). It is thus necessary to ensure to European industries the necessary time to find and develop (if at all possible) a substitute to DMF, as well as to leave them the time required to change all the industrial facilities. In fact the current industrial plants are not suitable for processes which use a different substance than DMF, and a long time would be necessary to adapt them, as well as huge investment. For example, for the use of DMF as solvent for acetylene, it would be necessary to change all cylinders in acetylene, that have a typical lifetime of 50 or more years, and that would have to be scrapped prematurely. The total population of acetylene cylinders in DMF service in Europe is estimated at more than 150 000. While for the production of synthetic and artificial leather, synthetic fibres, it would be necessary to change all the existing plants that strictly fit to the use of such a solvent, it would be necessary to change all the DMF recovery systems (such as distillation columns under vacuum). In addition, substitution may require adjustments of the pharmaceutical regulatory dossiers of the medicinal products resulting from the synthesis processes in which the solvents concerned are used. Replacement of a solvent optimised for	Thank you for your comment. Please refer to response to comment 2455 in this section.

			process reactions, yield and product purity, and controlled for workplace and environmental safety, can have the potential to substantially affect the impurity profile of the final drug substance or even the ability to successfully produce the drug substance. If a new solvent residue is present in a final drug substance, or if the impurity profile of the final drug substance is changed, the safety of the drug substance has to be re-established and approved by the EMA (European Medicines Agency). In addition, it has to be considered that DMF has many different uses and it could be, as a chemical, subjected to different legislations. Some of these required authorization/registration processes with the submission of the chemical dossiers to the Competent Authority. In these dossiers it was described the manufacturing process. If there will be a change in the manufacturing process, or DMF will be replaced by another substance, industries will have to review the dossier and in some cases the Competent Authority will have to evaluate and authorize again it. This happens for example with the biocidal products, and in a similar way with medicinal products.	
2286	2013/09/19 20:35	Company, Ireland	n/a	-
2285	2013/09/19 19:45	Individual, France	Diagnostica Stago wishes to comment on public consultation relating to a product made with DMF. See attachment confidential document.	Please refer to response to your comments in other sections.
2284	2013/09/19 19:31	Individual, France	Diagnostica Stago wishes to comment on public consultation relating to DMF. See attached confidential document.	Please refer to response to your comments in other sections.
2273	2013/09/19 16:05	EURATEX, Industry or trade association, Belgium	if textile coating is not exempted from authorisation a longer transitional period than the proposed 18 month is needed.	Thank you for providing your opinion.
2255	2013/09/19 12:39	Sweden, MemberState	We agree with the proposed dates.	Thank you for providing your opinion
2241	2013/09/18 14:58	Air Liquide Deutschland GmbH, Company, Germany	The sunset date should be established in such a way that the normal live-time of the cylinder receptacles, which are currently in service, are considered and therefore the standard sunset dates should be extended.	Thank you for your comment. Please refer to response to comment 2455 in this section.
2240	2013/09/18 14:50	Air Liquide Deutschland GmbH, Company, Germany	The sunset date should be established in such a way that the normal live-time of the cylinder receptacles, which are currently in service, are considered and therefore the standard sunset dates should be extended.	Thank you for your comment. Please refer to response to comment 2455 in this section.
2234	2013/09/17	Fedustria, Industry or trade	In case the use of DMF in the textile coating would not be	Thank you for your comment.

	16:11	association, Belgium	exempted from authorisation, the transitional period should be as long as possible. No alternatives Despite several years of investigation, no valuable alternative to replace DMF has been found to this day. The only possible alternatives are similar (aprotic) solvents that have a similar hazard classification as DMF. In addition, alternative solvents such as DMAC (with poorer results with regard to quality requirements) have already been recommended or are subject to authorisation. Other possible non aprotic solvents such as DMSO give rise to technical problems due to physical properties (freezing and boiling point) and corrosion to the existing equipment, quality requirements (light brown color of DMSO limits possibilities) and environmental issues such as higher energy use (higher boiling point), limited recovery of DMSO and smell. Water based polyurethane dispersions used to replace solvent based aromatic polyurethanes give poor results to quality requirements (such as thermoplastic behavior, chemical resistant to disinfection or sterilization) necessary for high performance technical textiles such as protective clothing. Other possible alternatives to aromatic polyurethanes give also poor results to quality requirements such as thermoplastic behavior. Textile coating producers have been using DMF for decades and over that period several coating properties have been improved step by step resulting in a better end use product. Some finished articles go into high tech and high protective applications (eg. medical health care, protective clothing, etc.). The specific requirements essential to such applications, e.g. chemical resistant to cleaning and disinfection, thermoplastic behavior, etc. can only be met by (aromatic) polyurethane coating for which DMF is an essential solvent. It is very unlikely that the same properties will and can be achieved in a very limited time frame hence if textile coating is not exempted from authorisation a longer transitional period than the proposed 18 month is needed.	Please refer to response to comment 2455 in this section.
2231	2013/09/17 11:34	Panasonic Industrial Devices Materials Europe GmbH, Company, Austria	Kindly refer to attached file	Please refer to response to your comments in other sections.
2214	2013/09/13 16:25	Company, United Kingdom	The use of a transitional period would only be valid if there are viable alternatives for DMF. The solvents which have the closest profiles are the other aprotic solvents such as DMAC and NMP;	Thank you for your comment. Please refer to response to comment

			however these are also subject to REACH legislation. Although all these products have a similar hazard profile they are currently being looked at independently and in a different way. It would be more consistent and logical to consider aprotic solvents as one class of materials and use the existing WEL approach to control them all.	2455 in this section. Also refer to response to your comment in section I.
2170	2013/08/28 12:56	Company, United Kingdom	At this stage, having read document 'Preparation of Draft Annex XIV entries for Substances recommended to be included in Annex XIV' dated 24th June 2013, we have no direct comments to make concerning the Transitional Arrangements detailed in Section 3.	Thank you for your comment.
2099	2013/06/25 10:35	Individual, France	no comments	-

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

#	Date	Submitted by (name, Organisation/MSCA)	Comment	Response
2488	2013/09/23 23:23	essenscia, Industry or trade association, Belgium	Opposite to the conclusion in the draft background document for DMF of 24 June 2013 point 2.4, we are of the opinion that specific Community legislation is in force that allows exemption of use from the authorisation requirement on the basis of Article 58(2) of the REACH Regulation. The risks to the environment are not the matter of concern according to ECHA's background document on DMF. The focus is on the health of workers. There is sufficient community legislation in place imposing the substitution principle and risk management measures relating to the protection of the workers: - Directive 98/24 on the protection of the health and safety of workers from the risks related to chemical agents at work ("the chemical agents at work Directive" or "CAD") CAD foresees the adoption by the Commission of occupational exposure limit values ("OELV"). DMF was included in the third list of indicative occupational exposure limit values (IOELVs) set up by Commission Directive 2009/161/EU (17.12.2009). IOELVs are health-based values derived from the most recent scientific data and correspond to threshold levels of exposure below which no detrimental effects are expected after short-term or daily exposure to the substance over a working life time. Member States were subsequently required to establish a national occupational exposure limit value, taking into account	Thank you for your comment. Please see response to comment 2456 (section I)

			the Community limit value of DMF by 18 December 2011. Therefore, Directive 2009/161/EU properly addresses the occupational use of DMF and health risk in connection with its use. - Council Directive 92/85/EEC (Pregnant Workers, Recently Given Birth or Breast Feeding), provides for additional necessary measures to be taken by the employer in case of risk or effect on the pregnancy or breastfeeding of a worker. Therefore, the use of DMF as an industrial process solvent in industrial installations, can be exempted from the authorisation requirements, in accordance with Article 58.2 of REACH.	
2473	2013/09/23 19:31	ChemSec, International NGO, Sweden	ChemSec supports the proposal of ECHA to not allow any exemptions.	Thank you for your comment.
2462	2013/09/23 18:21	Company, Portugal	The industrial use in closed systems(PROC 1, 2 or 3) should be exempted from authorization, since there is no exposure or limited and protected exposure to the substance.	Thank you for your comment. Please see response to comment 2456 (section I)
2456	2013/09/23 17:42	Company, Ireland	manufacture of pharmaceutical intermediates manufacture of active pharmaceutical ingredients. DMF is covered by the following community legislations:an OEL specified through directive 98/24/ec (chemical agents directive) and directive 2009/161/eu. Directive 92/85/ec (pregnant workers, recently given birth or breast feeding) provides the necessary measures to be taken by the worker. 2010/75/EU (industrial emissions directive) properly control the emission of DMF associated with the manufacture of APIs and the use of APIs during drug manufacture. The use of DMF is also controlled through the medicinal products directive 2001/83/ec and regulation (ec) no. 726/2004.	Thank you for your comment. Please see response to comment 2456 (section I)
2455	2013/09/23 17:38	European Diagnostic Manufacturers Association (EDMA), Industry or trade association, Belgium	EDMA does not support Authorisation as the most appropriate risk management option for the reasons mentioned under the 'General Comments' section. If the EU should regardless decide to proceed with including DMF on REACH Annex XIV, EDMA would request an exemption to use DMF as a process chemical. According to Article 58(2) of REACH: "[u]ses 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	Thank you for your comment. Please see response to comments 2456 and 2427 in section I.

			controlled." EDMA considers that ECHA should take into account the following directives as they represent specific Community legislation imposing minimum requirements for the protection of human health: 1. Council Directive 98/24/EC on the protection of the health and safety of workers from the risks related to chemical agents at work, in conjunction with Commission Directive 2009/161/EU establishing a third list of indicative occupational exposure limit values in implementation of Council Directive 98/24/EC and amending Commission Directive 2000/39/EC. Directive 98/24/EC establishes (Article 1(1)) "minimum requirements for the protection of workers from risks to their safety and health arising, or likely to arise, from the effects of chemical agents that are present at the workplace or as a result of any work activity involving chemical agents". Particularly, the Directive applies where (Article 1(2)) "hazardous chemical agents are present or may be present at the workplace". The minimum requirements of Directive 98/24/EC are established by introducing, amongst others, "indicative occupational exposure limit values for the protection of workers from chemical risks" (Article 3(2)). These limits are adopted at EU level; however, Member States should "take into account" (Article 3(3)) these indicative limit values when establishing national occupational exposure limit values. Directive 2009/161 lays down such specific limit values in its Annex. DMF is among the substances for which such specific limit values are established. Indeed, as highlighted by the Swedish Chemicals Agency in the Annex XV dossier to identify DMF as an SVHC, "DMF is included in the third list of indicative occupational exposure limit values (IOEL) set up by Commission Directive 2009/161/EU of 17 December 2009". 2. Council Directive 92/85/EEC 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 (tenth individual Directive within the meaning of Article 16 (1) of Directive 89/391/EEC). Directive 92/85 aims at encouraging "improvements in the safety and health at work of pregnant workers and workers who have recently given birth or who are breastfeeding" (Article 1(1)). It does so by providing that the Commission should "draw up guidelines on the assessment of the chemical, physical and biological agents and industrial processes considered hazardous for the safety or health of workers within" (Article	

			3(1)). These guidelines must serve as a basis for each employer to conduct an assessment on "the nature, degree and duration of exposure, in the undertaking and/or establishment concerned, of workers" (Article 4(1)). If the result of such assessment reveals a risk for the safety or health of workers, the employer shall "take the necessary measures to ensure that, by temporarily adjusting the working conditions and/or the working hours of the worker concerned, the exposure of that worker to such risks is avoided." In short, Directive 92/85 in conjunction with Directive 2009/161 establishes minimum requirements relating to the protection of human health resulting from the use of DMF. These requirements guarantee that the risks from the use of DMF are properly controlled, particularly when DMF is used at the workplace, or as a result of a work activity involving chemical agents. In this respect, EDMA notes that, having regard to the conclusions of ECHA's Draft background document for DMF, the main reason for prioritising DMF for inclusion in Annex XIV of REACH is the potential for significant workers exposure at some stages of the industrial processes. Therefore, while not supporting Authorisation as the most appropriate risk management option, EDMA considers that, should ECHA recommend the inclusion of DMF in Annex XIV of REACH, this should include an exemption for its use at the workplace, or as a result of a work activity. If the EU should regardless decide to proceed with including DMF on REACH Annex XIV, an exemption for PPORD up to 10 tons per annum would be required.	
2449	2013/09/23 17:05	Company, Germany	please refer to EDMA paper for full details. We request exemption for uses of DMF as a process chemical in the manufacturing of IVD. DMF can also be found as part of the final IVD product but the latter already benefits from an exemption from authorisation (article 60.2). As process chemical DMF is used in the manufacturing of chromogenic substrates used in IVD kits for the diagnosis/treatment of coagulation-related disorders. DMF is used in peptide synthesis which are essential functional reagents in immunoassays. strong solubilizer of small molecule antigens. no alternatives available. DMF has aN OEL set by the Chemical Agents Directive 98/24/ec. further legislations apply_ carcinogens and mutagens directive 2004/37/ec and council directive 92/85/eec	Thank you for your comment. Please see response to comment 2456 (section I). Note as DMF is not classified as a carcinogen or mutagen, Directive 2004/37/EC does not apply for this substance.
2448	2013/09/23	Vetex n.v., Company,	The use of DMF in textile coating should be exempted from authorization as there is sufficiently specific Community	Thank you for your comment.

	17:02	Belgium	legislation that covers this use and the risks are adequately controlled. Vetex n.v. is of the opinion that specific Community legislation is in force imposing the substitution principle and risk management measures relating to the protection of the workers and environment. Hence, this would allow exemption of use from the authorization requirement on the basis of Article 58(2) of the REACH Regulation. Protection of the health and safety of workers: DMF was included in the 3rd list of indicative occupational exposure limit values (IOELVs) set up by Commission Directive 2009/161/EU (17.12.2009). Member States were subsequently required to establish a national occupational exposure limit value, taking into account the Community limit value of DMF by 18.12. 2011. Therefore, Directive 2009/161/EU properly addresses the occupational use of DMF and health risk in connection with its use. Environmental protection: The management of Vetex n.v. is convinced that Directive 1999/13/EC on the limitation of emissions of volatile organic compounds due to the use of organic solvents in certain activities and installations establishes (VOC directive) the correct framework to guarantee that emissions form processes using DMF in the categories of activity described in Annex 1 (of Directive 1999/13/EC) are well controlled. The coating processes in the textile sector using DMF are explicitly mentioned in this annex. The VOC directive does not only set a strict emission limit value of 2 mg/Nm3 for VOC-discharges containing substances that carry the risk phrase R61 (as DMF does), it also obliges that substances or preparations containing VOCs with the risk phrases R61 shall be replaced as far as possible by less harmful substances or preparations within the shortest possible time (see article 5 point 6 of the VOC directive). The activities described in annex 1 of Directive 1999/13/EC are operated under conditions guaranteeing controlled exposure (public health and the environment). Monitoring and reporting obligations for companies as well as for member states are part of the directive. In our view, the VOC-Directive has the same objective as what is intended by authorization (replacing by less harmful substances) under REACH, there is no need at all to apply additional obligations to DMF. This very same obligation exist already for years under EU-legislation. The requirement to apply for an authorization will hence not improve the protection of the environment or the workers. As authorization is not only a burdensome procedure but also	Please see response to comments 2456 and 2488 in section I.

			very costly for the textile coating industry that consists mainly of SME, this will result in an additional impediment of the competitiveness with regard to the non-European enterprises. Therefor the management of Vetex n.v. is of the opinion that textile coating as described in annex I of the directive 1999/13/EC (i.e. "any activity in which a single or multiple application of a continuous film of a coating is applied to textile and fabric …") should be exempted from authorization.	
2441	2013/09/23 16:23	DINOX Handels-GmbH, Company, Germany	All industrial uses, as they are already adequately controlled.	Thank you for your comment. Please see response to comment 2456 (section I).
2434	2013/09/23 15:51	EFPIA, Industry or trade association, Belgium	The use of DMF in the manufacturing of pharmaceutical 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 is exempted from REACH authorisation requirements. This exemption would also include all PPORD uses of DMF (up to 50ts/pa) in the production of medicinal and veterinary products. Rationale for the Request for an Exemption as per Art 58(2): As we are all aware, a directive is a legal instrument provided for in the EU Treaty and to date the majority of Community HSE legislation is based on the choice of the directive as the most appropriate legal instrument. It is binding in its entirety and obliges Member States to transpose it into national law within the deadlines clearly set out in the directive. A directive enters into force once it is published in the Official Journal of the EU. EU directives on safety and health at work have their legal foundation in Article 153 of the Treaty on the Functioning of the European Union (ex Article 137 TEC), which gives the EU the authority to adopt directives in this field. A wide variety of EU directives setting out minimum health and safety requirements for the protection of workers have since been adopted. Member States are free to adopt stricter (but not less strict) rules for the protection of workers when transposing EU directives into national law, and so legislative requirements in the field of safety and health at work can vary across EU Member States. The decision to recommend DMF for inclusion in Annex XIV is based solely on occupational health risks (DMF is classified as toxic for reproduction category 1b). Those risks are already properly controlled (as outlined below) by the application of Directive 98/24/EC (Chemical Agents Directive), Directive 2009/161/EU (IOEL for DMF), Directive 92/85/EC (Pregnant	Thank you for your comment. Please see response to comment 2456 (section I).

			Workers), Directive 2010/75/EU (Industrial Emissions Directive) and 2001/83/EC (Medicinal Products Directive) which impose minimum requirements that must be transposed into national legislation by EU Member States (quotations from legislation is given below in italics) 98/24/EC Chemical Agents Directive (CAD) Article 1 of Directive 98/24/EC This Directive ..... lays down minimum requirements for the protection of workers from risks to their safety and health arising, or likely to arise, from the effects of chemical agents that are present at the workplace or as a result of any work activity involving chemical agents. Article 6(2) of Directive 98/24/EC Substitution shall by preference be undertaken, whereby the employer shall avoid the use of a hazardous chemical agent by replacing it with a chemical agent or process which, under its condition of use, is not hazardous or less hazardous to workers' safety and health, as the case may be. Where the nature of the activity does not permit risk to be eliminated by substitution, having regard to the activity and risk assessment referred to in Article 4, the employer shall ensure that the risk is reduced to a minimum by application of protection and prevention measures, consistent with the assessment of the risk made pursuant to Article 4. These will include, in order of priority: • Design of appropriate work processes and engineering controls and use of adequate equipment and materials, so as to avoid or minimise the release of hazardous chemical agents which may present a risk to workers' safety and health at the place of work; • Application of collective protection measures at the source of the risk, such as adequate ventilation and appropriate organizational measures; Where exposure cannot be prevented by other means, application of individual protection measures including personal protective equipment. 1. We believe ECHAs previous interpretation of the minimum requirements (RCOM DMAC) as outlined in CAD is contrary to the principles of proportionality. The legal obligation on the employer to put in place specific protection and prevention measures is in keeping with the principles of proportionality. A technical feasibility assessment of control measures beyond what is recommended by a chemical agents risk assessment is disproportionate. Note the clear intentions of CAD: "To ensure not only the protection of the health and	

			safety of each individual worker but also to provide a level of minimum protection of all workers in the Community which avoids any possible distortion in the area of competition" (Preamble 4 of Directive 98/24/EC) 2009/161/EU Indicative OEL Values Directive Article 2 of Directive 2009/161/EU Member States shall establish national occupational exposure limit values for the chemical agents listed in the Annex, taking into account the Community values. 1. 98/24/EC (CAD) requires setting of indicative occupational exposure limit values (IOELVs) in all Member States (who are obligated to do transpose this and that their national limits must, at a minimum, be as stringent as the EU levels). DMF is referenced in Directive 2009/161/EU, establishing a third list of indicative occupational exposure limit values in implementation of Council Directive 98/24/EC and amending Commission Directive 2000/39/EC The following OEL has been set for DMF within EU law: 8 hour TWA: 5 ppm (15mg/m³), STEL (15 mins): 10 ppm (30mg/m³). Austria, Belgium, France, Germany, Ireland, Italy, Netherlands and UK are, to name but a few, Member States that have transposed this OEL into their National Legislation. ChemLeg members across various EU Member States have actual DMF monitoring data that can be shared with ECHA to show the controls used within our manufacturing facilities enables us to comply with the DMF OEL. 2. Furthermore, "A registrant is allowed to use an IOEL as a DNEL for the same exposure route and duration, unless new scientific information that he has obtained in fulfilling his obligations under REACH does not support the use of the IOEL for this purpose." [ECHA Guidance Chapter R.8: Characterization of dose [concentration]-response for human health p. 137]. According to the ECHA guidance, IOEL values are valid DNELs to be accepted for occupational uses. If the CMR properties were considered when deriving the IOEL, there is no scientific reason for ECHA not to accept the IOEL unless new experimental data has been generated. In Summary: DMF is referenced in 2009/161/EU and has been given a minimum OEL. Therefore 2009/161/EU should satisfy Art 58(2) Existing Community Legislation. Not accepting this Directive as satisfying the requirements for an exemption under Article 58(2) undermines the legal authority of Directive 2009/161/EU	

			and creates a situation of double regulation which is against the principle of the EU Commission's approach to "Smart Regulation". ChemLeg members have data to show existing OEL for DMF is complied with at API Manufacturing facilities across various Member States. 92/85/EC Pregnant Workers, Recently Given Birth or Breast Feeding Article 5 • If the results of the assessment referred to in Article 4 (1) reveal a risk to the safety or health or an effect on the pregnancy or breastfeeding of a worker within the meaning of Article 2, the employer shall take the necessary measures to ensure that, by temporarily adjusting the working conditions and/or the working hours of the worker concerned, the exposure of that worker to such risks is avoided. • If the adjustment of her working conditions and/or working hours is not technically and/or objectively feasible, or cannot reasonably be required on duly substantiated grounds, the employer shall take the necessary measures to move the worker concerned to another job. • If moving her to another job is not technically and/or objectively feasible or cannot reasonably be required on duly substantiated grounds, the worker concerned shall be granted leave in accordance with national legislation and/or national practice for the whole of the period necessary to protect her safety or health. • The provisions of this Article shall apply mutatis mutandis to the case where a worker pursuing an activity which is forbidden pursuant to Article 6 becomes pregnant or starts breastfeeding and informs her employer thereof. 1. Directive 92/85 provides for the necessary measures to be taken by the employer in case of risk or effect on the pregnancy or breastfeeding of a worker In Summary: Some active pharmaceutical ingredients by the very nature of their pharmacological action are Reprotoxins e.g. antimitotic drugs. Bulk API plants handling these substances (such as DMF) typically have reproductive hazard evaluation programmes in place covering APIs and solvents to protect the employee planning a pregnancy or recently become pregnant. Examples of risk reduction recommendations include additional PPE, delegating tasks to non-pregnant employees or banning such workers entering areas where DMF type substances are	

			handled. Therefore 92/85/EC should satisfy Art 58(2) Existing Community Legislation 2010/75/EU Industrial Emissions Directive IED Art 58: Substitution of Hazardous Substances Substances or mixtures which, because of their content of volatile organic compounds classified as carcinogens, mutagens, or toxic to reproduction under Regulation (EC) No 1272/2008, are assigned or need to carry the hazard statements H340, H350, H350i, H360D or H360F, shall be replaced, as far as possible by less harmful substances or mixtures within the shortest possible time IED Art 59(5) Control of Emissions: The emissions of either volatile organic compounds which are assigned or need to carry the hazard statements H340, H350, H350i, H360D or H360F or halogenated volatile organic compounds which are assigned or need to carry the hazard statementsH341 or H351, 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 set out in Part 4 of Annex VII . 1. DMF is used in Bulk Pharma manufacturing facilities to manufacture API; all Bulk Pharma API manufacturing facilities are required to have a PPC Permit (soon to be Industrial Emissions Permit under the Industrial Emissions Directive). This requirement is referenced in Annex I of the IED (section 4.5). 2. The IED (and the previous directives that have now been included within it including 2000/76/EC) requires permit holders who use H360D compounds to replace them, as far as possible, by less harmful substances within the shortest period of time. DMF is a H360D substance 3. The IED requires permit holders that emissions of H360D substances shall be controlled under contained conditions as far as technically and economically feasible to safeguard public health and the environment. DMF is a H360D substance. 4. DMF used in the API manufacturing stage is collected after use and (in the majority of cases) is incinerated (under the Waste Incineration Directive 2000/76/EC soon to be incorporated into the Industrial Emissions Directive). Where DMF is not incinerated, it is recycled. In Summary: All bulk API facilities using DMF must have an Industrial Permit to operate. That permit lays down minimum conditions to	

			protect the environment as well as requiring substitution of H360D substances. The EU Commission does not need to implement further legislation to require the substitution of H360D substances (that are used in an IED permitted facility). All waste DMF is handled appropriately. Community Legislation (2010/75/EU) properly controls the emissions of DMF associated with the manufacture of APIs and the use of the API during drug manufacture. Therefore 2010/75/EU should satisfy Art 58(2) Existing Community Legislation 2010/75/EU Industrial Emissions Directive (Solvents) IED Annex VII Technical Provisions relating to Installations and Activities using Organic Solvents Part 1(Activities): (8). Manufacturing of pharmaceutical products: The chemical synthesis, fermentation, extraction, formulation and finishing of pharmaceutical products and, where carried out at the same site, the manufacture of intermediate products IED Annex VII Technical Provisions relating to Installations and Activities using Organic Solvents Part 2(Thresholds and Emission Limit Values): (20). Manufacturing of pharmaceutical products: >50ts/yr. of solvents; waste gases emission limit 20mg/m³; total ELV is 15% of solvent output IED Art 59(1) Control of Emissions: Member States shall take the necessary measures to ensure that each installation complies with either of the following: (a) the emission of volatile organic compounds from installations shall not exceed the emission limit values in waste gases and the fugitive emission limit values, or the total emission limit values, and other requirements laid down in Parts 2 and 3 of Annex VII are complied with Existing Community Legislation (2010/75/EU) properly controls the emissions of DMF associated with the manufacture of APIs and the permitting/use/storage of the solvent during drug manufacture. One objective of the IED is to prevent or reduce the direct and indirect effects of emissions of VOCs during the manufacture of pharmaceutical products into the environment, mainly into air, and the potential risks to human health, by providing measures and procedures to be implemented for certain activities. The IED already governs and manage the risks that the inclusion of Pharma uses of DMF in REACH Annex XIV seeks to manage. Article 62 (5b) of the REACH Regulation would suggest that this is also the case. In Summary: All bulk API facilities using >50ts/yr. of solvents (including DMF)	

			must have an Industrial Permit to operate. That permit lays down maximum emission to air limits for solvents, therefore the IED provides minimum emission to air standards in API Bulk Manufacturing facilities using >50ts/yr. of solvents. This shows that DMF is properly controlled. Therefore 2010/75/EU should satisfy Art 58(2) Existing Community Legislation Medicinal Products Directive: Directive 2001/83/EC & Regulation (EC) No 726/2004 1. The EU medicinal regulatory system protects public health and secures the availability of medicinal products for EU citizens by requiring all such products to have been granted a Marketing Authorisation (MA) of before they are placed on the EU market. These MAs are granted only if the manufacturing process complies with the EU quality standards known as "good manufacturing practices." After a MA is issued, MA holders may not introduce any changes into the manufacturing process without the consent of the Member State competent authority (The rules on marketing authorization are found primarily in Directive 2001/83/EC of the European Parliament and of the Council Directive 2001/83/EC of 6 November 2001on the Community code relating to medicinal products for human use, OJ L 311, 28.11.2001, p. 67–128 and 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, OJ L 136, 30.4.2004, p. 1–33 (together the "Medicinal Products Legislation"). Directive 2001/83/EC, Article 23). Finally, once a medicinal product has been authorised and placed on the EU market, its safety is monitored throughout its entire lifespan to ensure that, in case of adverse reactions that present an unacceptable level of risk under normal conditions of use, it is rapidly withdrawn from the market (European Commission Website, DG Health & Consumers, Public health, Medicinal products for human use available at: http://ec.europa.eu/health/human-use/index_en.htm last visited on May 30, 2013). This is done through the EU system of "Pharmacovigilance" set out in the Medicinal Products Directive (MPD). 2. We believe that the MPD does properly control the risks of the use of DMF within the manufacture of an API that 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 MA of a medicinal product referred to in	

			Article 40 of Directive 2001/83/EC is obliged "to comply with the principles and guidelines of good manufacturing practice (GMP)" as laid down by community law. Principles and guidelines of GMP require impurity testing of pharmaceutical ingredients to ensure that specific threshold limits for residual solvents are met. All Pharmaceutical products that are impacted by such solvents have the information included in the MA which can be withdrawn if the pharmaceutical product does not meet the residual solvent specification. This concentration limit is enforced via the Member State relevant Health Regulator (e.g. MHRA in the UK). EMA guidance on residual solvents (EMA/CHMP/ICH/82260/2006) contains specific limits for DMF (PDE 8.8mg/day and 880ppm). 3. Since the residual amount of DMF in the eventual pharmaceutical product is safety-limited by the EMA (Guideline for Residual Solvents in practice virtually all the DMF used during manufacture of the API would be present in the waste streams that are then disposed of via incineration as hazardous waste (under the Waste Incineration Directive 2000/76/EC soon to be incorporated into the Industrial Emissions Directive). Where DMF is not incinerated, it would be purified and recycled into DMF that can be used again. 4. Recital 111 of REACH cautions against mixing the policy aims of REACH with the policy aims of the European Medicines Agency (EMA). The legislative history of REACH reflects the special relationship between the chemical and medicinal regulatory regimes. The Commission expressly addressed the interaction between the two regimes when it proposed REACH, indicating how it would avoid potential overlaps (thereby showing that the Commission was (i) aware of the potential overlap between REACH and the medicines legislation and (ii) it aimed to avoid such overlap): "Certain uses of substances are not subject to authorisation because their human health and environmental effects are considered to be addressed by equivalent Community legislation. It would be unreasonable to subject such uses to two systems with the cost and resources this would imply. The Commission will propose a modification of the legislation on medicinal products for human use and veterinary use respectively to address risks related to the environment. This will be part of the benefit/risk assessment which has to be positive as a prerequisite for approval of the medicinal product". [Emphasis added] In Summary:	

			Firstly, the REACH Regulation was not meant to overlap with or impede the functioning of this Medicinal regulatory regime. Indeed, substances used in medicinal products for human and veterinary use and falling under the scope of the Medicinal Products Legislation are specifically exempted from the REACH authorisation requirements. Secondly, in line with the text of REACH, the history of the Regulation, and the proportionality principle, we believe that ECHA should avoid any conflict with the EMA's specific authority to approve the market placement of medicinal products. Thirdly, 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). Therefore 2001/83/EC and its associated Guidance should also help satisfy our compliance with the conditions for exemption set down in Art 58(2) with regard to existing Community Legislation. Conclusions: • In the comments above, we have cited various EU laws which, collectively and individually, meet the conditions imposed for the exemption under Article 58.2 of REACh • 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, not only by REACh 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… • Pharmaceutical manufacturing uses of DMF meet the requirements set out in Article 58 (2) of REACH and on this basis, should be exempted from REACH Authorisation requirements; • Our uses of DMF as an aprotic solvent are already governed by existing EU legislation setting minimum requirements for the proper control of risks to human health or the environment;	

			• There will be no direct or net environmental benefit by including Pharma uses of DMF in Annex XIV; • Use of DMF in pharmaceutical manufacturing is not widely dispersive, and the scoring system applied in Annex XV would not qualify DMF as used in Pharma for prioritization • REACH article 62(5)(b)(i) suggests that an Annex XIV listed substance handled in a facility that is permitted by Directive 96/61/EC (soon to be incorporated into 2010/75/EU IED) doesn't need to consider risks from Human Health or the Environment when submitting an application for an Authorised Use of that Substance. This therefore exempts annex XIV listed substances from Authorisation if the substance is used in an IPPC Permitted facility and no economic or technically feasible substitution substances exist NOTE: DMF belongs to a class of "aprotic solvents" which also includes the solvent N,N-dimethylacetamide (DMAC). It should be noted that the proposed listing of DMAC on Annex XIV is currently subject to discussions between representatives of the pharmaceutical industry and the authorities, both on CA level in the Member States and on EC level. The arguments provided on DMAC from the EU Pharma ChemLeg Group are similar to the ones discussed in this consultation response.	
2431	2013/09/23 15:37	GIFAS, Industry or trade association, France	Please refer to attached document	Thank you for your comment. Please see response to comment 2456 (section I). Please also refer to the answer to your comment in section I, general comments.
2425	2013/09/23 15:08	VOWALON Beschichtung GmbH , Company, Germany	DMF ist das wichtigste Standardlösungsmittel für Polyurethan-Granulate. (Lösungsmittel wie N-Methylpyrrolidon ist ebenfalls als Gefahrstoff eingestuft.) Bei der Verwendung von DMF werden alle arbeitsschutzrechtlichen Vorschriften eingehalten (z.B. eingehauste Beschichtungseinheiten, Absaugeinrichtung, Themische Nachverbrennung, Ex-geschützte Mischerei, jährliche Überprüfung der Mitarbeiter durch die Betriebsärztin, persönliche Schutzausrüstung für Mitarbeiter). Bei Einsatzbeschränkungen von DMF könnten keine lösemittelbeständigen PUR-Beschichtungen für Schutzkleidungen und Hygeineartikel mehr hergestellt werden. Alternative wässrige Beschichtungen werden zur Zeit intensiv im Rahmen von Forschungs-Kooperationen entwickelt und	Thank you for your comment. Please see response to comment 2456 (section I).

			getestet. Die Eigenschaftsbilder entsprechen noch nicht den oben beschriebenen Sachverhalten. Die Überprüfung des Restgehlates an DMF in PUR Beschichtungen auf der Basis von DMF-Granulatlösungen ergab eine deutliche Unterschreitung des SVHC Grenzwertes von 0,1% im Fertigprodukt. Somit geht keine potentielle Gefahr für den Endverbraucher aus.	
2423	2013/09/23 15:01	Company, Czech Republic	The intermediates are obtained and used under strictly controlled conditions according to article 18 Regulation (EC) No 1907/2006 in which is rigorously contained by technical means during its whole lifecycle. For these reasons, in all the three fields of application mentioned above the DMF is introduced into the reactors via transfer systems designed to minimize environmental release, by trained personnel, and is thus contained within the process stream. In practice all the DMF used during manufacture (in closed systems) is captured in waste streams which are typically combusted under strictly controlled conditions in order to destroy all residual DMF. Controls conducted by industries in the workplace demonstrate how the concentrations of DMF are far below the TLV-TWA equal to 15 mg/m3. Periodic analysis on workers confirms the lack of exposure to DMF and the efficiency of prevention measures adopted. The use of DMF to produce fine chemicals and medicinal products works similarly. Using the first category as an example, we see that DMF is mostly used as polar aprotic solvent (e.g. nucleophilic substitution) in the synthesis of active pharmaceutical ingredients (APIs) and associated intermediates. DMF offers generally high solubility of many APIs and intermediates and sufficient solubility of many inorganic reagents (e.g. acids and bases). Furthermore, DMF has a high boiling point (153oC), low vapor pressure, and is soluble in water. Because of these characteristics DMF is an essential and highly specific solvent within the processes used by pharmaceutical industries.	Thank you for your comment. Please see response to comment 2456 (section I).
2418	2013/09/23 14:26	Hungarian Pharmaceutical Manufacturers Association, Industry or trade association, Hungary	According to directive 2009/161/EU, the occupational exposure limit is 15 mg/ m³ (8-hr Time Weighted Average) for DMF. This IOEL has been adopted by most EU MS's, including Hungary (25/2000. (IX. 30.) EüM–SZCSM együttes rendelet a munkahelyek kémiai biztonságáról). As it is explained previously at the general comment section, uses where the exposure limit is lower than the IOEL, should be exempted from the authorization process. Use of DMF for the manufacturing of active pharmaceutical ingredients is performed within enclosed equipment in	Thank you for your comment. Please see response to comment 2456 (section I)

			accordance with Good Manufacturing Practices (GMP). DMF (and other solvents) are introduced into the reactors via closed transfer systems designed to minimize environmental release, by trained personnel, and are thus contained within the process stream. In practice virtually all the DMF used during manufacture is present in waste streams which are incinerated under strictly controlled conditions. Categories belonging to our pharmaceutical uses: SU3, PROC 3, PROC 8b, PROC 4, ERC 4 SU3, SU24, PROC 15, PC21, ERC4 Detailed description of our uses: Supply of DMF as a bulk solvent to manufacturing facility involve the following distinctive steps: • Sampling from the road tanker (quality reasons): A closed system has been established for the task. The necessary sample amount (usually less then 1 l/case) is taken with the help of vacuum and a special sampling fitting without any spillage or splashing. • Sample analysis: Sample preparation is performed under fume cupboard. The analysis is performed mainly in closed system (gas chromatography) efficiency of the closeness of the cupboards are measured, monitored and documented during the revisions and it is controlled by an SOP. • Transfer of substance from road tanker to dedicated storage tank via contained piping. The intermediate arrives at the sites in closed tank containers. The tanks are unloaded at a dedicated unloading station, with a retention basin. The transfer to the storage tank from the tank container is performed with flexible hoses with camlock connections. After the operation and before disconnection, the residue in the hose is flushed out with nitrogen. The hoses are stored in closed storage tubes. There is a written procedure and training for the task. A vapour return line is used for the unloading, which ensures that no vapors will be emitted into the environment. • After the transfer to the plants storage tanks, the transfer of DMF is performed in a closed system, with the help of vacuum, pressure and pumps. • Sampling of the reactors are performed via a closed loop system Transfer of liquid waste stream from reaction vessels via contained piping to dedicated storage tanks. • The Member Companies of The Hungarian Pharmaceutical Manufacturers Association have the required	

			IPPC licence, which proves that the technical level of the site fully fulfills the demands of the IPPC directive, and performers the requirements of BAT (best available technology). • Periodic cleaning and maintenance works under strictly controlled conditions. Special procedures applied before cleaning and maintenance. Every intervention is managed through a working permit which must include: - The description of the task to do - The identification of hazards relative to product & equipment - The necessary preparation prior to start task (draining, cleaning) - The risk analysis which defines individual protective equipment if needed. Every intervention which requires opening of an equipment compulsory has: - Log-Out – Tag-Out procedure for the machines - The implementation of 2 physical barriers to prevent contact with the product - Draining, cleaning - Specific personal protective equipment Every intervention which requires penetration into an equipment compulsory requires a specific authorization which includes: - The implementation of 2 physical barriers to prevent contact with the product - Draining, cleaning of the equipment - A control to check absence of residue - A control to check the atmosphere prior penetration - Specific personal protective equipment The goal of these SOPs is to be sure any contact between the product and the operator, who cleans or maintains the equipment may occur. If bulk storage supply is not a feasible option, exposure potential is minimized whilst emptying drums via a dip pipe into the reaction vessel: • Dip pipe is attached to drum via a high integrity closed coupling during liquid transfer, • An extracted sleeve is attached to dip pipe to prevent drips and leaks when it is removed from the drum, • A suitable key is provided for removing and replacing the drum stopper. Risk management measures in place to control releases from	

			the use(s) or categories of uses of DMF The Member Companies of The Hungarian Pharmaceutical Manufacturers Association have strong inner action plans to minimize exposure. Our inner OEL band system is usually specifies equal or stronger acceptable exposure levels than the national regulations. There is an industrial hygiene plan for yearly measurements of possible exposure in the plant. In case of any limit exceed, an action plan is made to technically minimize exposure. For the protection of workers, the information of hazards are estimated by the substances phys-chem properties, the substances quantity, the frequency of use, the time of the operation, and the closeness of the system. The critical points are investigated, and there is an action plan to technically minimize exposure. For CMR compounds such as DMF, we have a strict inner Standard, Guide and SOP for the handling of the substances .We also apply to reprotoxic substances the same strict requirements as for the exposure controls for carcinogenic and mutagenic substances.	
2415	2013/09/23 14:02	Individual, Italy	DMF is used as a solvent for the production of intermediates that find application in the area of pharmaceuticals, biocides, plant protection, fragrances and fine chemicals. The use of DMF as a solvent in the production of intermediates, which are subsequently used to synthesize APIs (Active Pharmaceutical Ingredients) is carried out within enclosed equipment in agreement with the Good Manufacturing Practices (GMP). In the case of fragrances and fine chemicals, the intermediates, in accordance with the REACH Regulation, shall be synthesized and used (transformed) under strictly controlled conditions in that it is rigorously contained by technical means during its whole lifecycle. Finally, with respect to the biocides and plant protection area (i.e. synthesis of intermediate used to manufacture an active substance) applies the same logic described above for "Fine Chemicals". For these reasons, in all the five fields of application cited above, DMF is used under strictly controlled conditions. In general, it is introduced into the reactors by means of a dedicated automated closed system, designed to minimize environmental release and to exclude the exposure for the workers, by trained personnel. The DMF is recovered from the apparatus of reaction by means of a liquid ring vacuum pump,	Thank you for your comment. Please see response to comments 2456 and 2365 in section I. In addition, in relation to biocides, 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 was repealed by Regulation (EU) 528/2012 (Biocidal Product Regulation) from 1 September 2013. This Regulation includes a risk assessment and authorisation procedure for active substances and products containing these substances. DMF does not seem to be approved as a biocidal active substance or included in the review programme under the

			sent to the refrigerating system and recycled to the reactors. The exhaust DMF and he waste streams are typically managed under strictly controlled conditions and in agreement with the international and local norms for the treatment of the waste. To conclude, Endura is convinced that DMF, when used as a solvent for the production of intermediates automatically, implies the minimization and control of the exposure for the workers and excludes the release in the environment during its whole lifecycle (including the management of the waste generated). For this category of use the risk is properly controlled and does not constitute danger for people and environment.	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". 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 DMF. Therefore, this legislation may not be regarded as a sufficient basis for exempting this use of DMF from authorisation in accordance with Article 58(2) of the REACH Regulation.
2414	2013/09/23 13:38	Company, Germany	Abbott anticipates that its use of the substance DMF in the production and subsequent use of medical devices and IVDs regulated under Directives EC Nos. 93/42/EEC and 98/79/EEC will be exempted from the requirements of Authorisation in accordance with article 60(2) of REACH, however exemptions are requested for the following other associated uses of the substance. Exemptions requested under Article 56(3): Clinical Chemistry and Quality Control Testing DMF is used as a solvent in test reagents used for the quality control testing of materials and components used during manufacture of in vitro diagnostic reagents. DMF is also specified in many analytical tests that are required by the EU Pharmacopeia (see list in confidential attachments). It is also used in stock solutions used in the preparation of labelled probes and conjugates and for the storage of labelled compounds prior to further formulation into diagnostic reagents. We consider that article 56(3) of REACH that exempts substances listed on Annex XIV from the requirements of Authorisation where the use is for scientific research and development, applies to analytical and quality control uses for	Thank you for your comment. Please see response to comment 2456 (section I). In addition, regarding the Medical Devices Directive (MDD, Directive 93/42/EEC) - this Directive 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: 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

			instance in use in medical laboratories where the diagnostic technique specifies the use of the substance. These uses are carried out in laboratory settings under controlled conditions (as detailed in the IVD and Medical Device Directives) and in quantities of less than 1 tonne per year.	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.
2411	2013/09/23 13:31	Company, Finland	- The use of N-dimethylformamide (DMF) as solvent in synthesis of Active Pharmaceutical Ingredients (API) should be exempted from the authorization requirement. - The exposure for workers of DMF is already prevented in the API production, as the purity requirements of the product provide for isolation. - The substitution to possible alternatives in pharmaceutical products requires firstly an extensive research and development and secondly a long process for products approval. The possible alternatives are aprotic solvents as N-methyl	Thank you for your comment. Please see response to comment 2456 (section I).

			pyrrolidone or N,N- dimethyl acetamide, which are already in the candidate list, and may well be prioritized for authorization, if their volumes increase. - When authorization is required, the drafting of the substitution plan is very challenging due to the fact, that alternatives already are identified as SVHC-substances. - When authorization is required for API-synthesis, some of the production may be ceased. The APIs withdrawn from the market due to cost reasons may play an important role in providing variety for example to cancer treatments. The authorization for APIs may thus affect patient health. - The costs of authorization process are anyhow transferred to the prices of pharmaceutical products, which may further challenge the already difficult situation of people needing them - DMF is not present in the final pharmaceutical products. If pharmaceutical industry in the European Union is facing the authorization process, the production of those API:s that need DMF as solvent may be transferred outside EU. Conclusion: DMF is already used in API synthesis under strictly controlled conditions and the exposure to workers is prevented. The authorization process does not lead to increased safety, but only leads to excess costs and use of manpower both in pharmaceutical industry and in authority. If authorization is not applied, the patient health may be endangered and the production transferred outside EU.	
2381	2013/09/23 11:06	Company, Ireland	At Astellas Dublin Manufacturing Plant, three of the four manufacturing processes utilize DMF as a key polar aprotic solvent to support reactions for the manufacture of three Active Pharmaceutical Ingredients (API's). The use of DMF affects the rate of the reaction and it also has the ability to minimise the formation of side products thus allowing us to produce high quality API's. No comparable performance with any other solvent is known to us except possibly (but quite potentially also unlikely) for similar polar aprotic solvents with similar physical or chemical properties and similar or greater environmental, occupational health, or other concern. Work to identify alternatives to DMF in the manufacture of pharmaceutical products within the EU has been undertaken in the past with very limited success. Significant development work would be required to identify and validate viable alternatives involving major changes to the manufacturing processes and the Marketing Authorisation. Given the complexity of global supply chains, the ability of Astellas, Dublin	Thank you for your comment. Please see response to comment 2456 (section I).

			Plant to secure a continuous supply of medicines to the market could be at risk if DMF was not available for use. Astellas requests that the use of DMF in the manufacturing of pharmaceutical products as defined in Art. 1(2) of the Directive 2001/83/EC relating to medicinal products for human use as defined in Art. 1(2) Directive 2001/82/EC for medicinal products for animal use is exempted from REACH authorisation requirements. This exemption would also include all PPORD uses of DMF (at our facility this is up to 5ts/pa). DMF is used at our site in closed systems with only occasional, very limited opportunity for exposure e.g. during sample taking (PROC 3) and monitoring data have confirmed that levels are close to the limit of detection or less. The risks of environmental exposure of DMF 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 safety and environmental systems. Destruction of liquid waste solvents is by incineration, and is 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 Exemption from authorisation is requested for the use of N,N-Dimethylformamide (CAS 200-679-5) 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. 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. In summary, we believe that this exemption should be granted because of the following key reasons: • The decision to recommend DMF for inclusion in Annex XIV is based solely on occupational health risks (DMF is classified as toxic for reproduction category 1B). Those risks are	

			already properly controlled by the application Directive 92/85/EC (Pregnant Workers). Examples of risk reduction recommendations include additional PPE, delegating tasks to non-pregnant employees or banning such workers entering areas where DMF type substances are handled. Therefore 92/85/EC should satisfy Art 58(2) Existing Community Legislation • Community Legislation (compliance with the Chemical Agents Directive (98/24/EC)) relating to the Health, Safety and Environmental (HSE) control of DMF already exists in particular community legislation relating to Occupational Exposure Levels. We have DMF OEL monitoring data taken from various areas across the site which can be shared with ECHA on request from ECHA. According to the ECHA guidance, IOEL values are valid DNELs to be accepted for occupational uses. If the CMR properties were considered when deriving the IOEL, there is no scientific reason for ECHA not to accept the IOEL unless new experimental data has been generated. • Residual amounts of DMF in the eventual pharmaceutical product are safety-limited by the ICH Q3C (Guideline for Residual Solvents). So in practice, virtually all the DMF used during manufacture is present in the waste streams (other than that lost through evaporation) which is primarily disposed of via incineration. We have an IPPC licence to operate (Directive 96/61/EC). This licence lays down minimum conditions to protect the environment as well as requiring substitution of H360D substances. The EU Commission does not need to implement further legislation to require the substitution of H360D substances . Community Legislation (2010/75/EU) properly controls the emissions of DMF associated with the manufacture of APIs and the use of the API during drug manufacture. Therefore Directive 96/61/EC and 2010/75/EU should satisfy Art 58(2) Existing Community Legislation. • Substituting a solvent used in the manufacture of a commercially available Pharmaceutical Product may require additional human and animal testing (contrary to the principles of REACH); • Substituting a solvent used in the manufacture of a commercially available Pharmaceutical Product requires the current Marketing Authorisations (granted by the European Medicines Agency (EMA)) to be amended leading to excessive costs (3M – 12M EUR per product) and time delays. The mission of the EMA is to authorise and supervise medicinal products for human and veterinary use. It would be important not to create	

			conflict with the mission of this body who were established by Regulation (EC) No 726/2004. Conclusions Our uses of DMF as an aprotic solvent are already governed by existing EU legislation setting minimum requirements for the proper control of risks to human health or the environment; In the comments above, we have cited various EU laws which, collectively and individually, meet the conditions imposed for the exemption under Article 58.2 of REACH. 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. Pharmaceutical manufacturing uses of DMF meet the requirements set out in Article 58 (2) of REACH and on this basis should be exempted from REACH Authorisation requirements.	
2374	2013/09/23 10:01	Company, Sweden	Uses of DMF as a solvent or processing aid in the manufacture of medicinal products should be exempt from authorization because community-wide measures exist to limit work-place exposure. N,N-dimethylformamide (DMF) is one of a class of extremely useful aprotic solvents. The physical properties of these solvent makes them an attractive choice from a chemistry perspective in the synthesis of Active Pharmaceutical Ingredients (APIs) and associated intermediates. Other aprotic solvents with the same physical properties are N, N-dimethlyacetamide (DMAc), N-methyl-pyrrolidone (NMP), N-methylformamide and N-methylacetamide. These properties which facilitate certain chemical reactions, use as catalyst or in separation and purification processes within organic chemistry, are not possible to obtain with other types of solvents. However, they all show the same intrinsic properties with regards to reproductive toxicity, making them infeasible as an alternative for DMF as solvent. Finally, some of the aprotic solvents are already on the candidate list and those currently not on the list would most likely be added in the future making a substitution unachievable. When DMF is used in the manufacture of Active Pharmaceutical Ingredients (APIs) and associated intermediates these processes are performed batch wise in enclosed reactor systems with minimal or no exposure of solvents or substances in accordance with Good Manufacturing Practices (GMP). DMF is introduced under controlled conditions into the reactors via transfer systems designed to minimize environmental release and by trained personnel using appropriate protective	Thank you for your comment. Please see response to comment 2456 (section I) and to comment 2368 in this section.

			equipment. In practice virtually all the DMF used during manufacture would be present in the waste streams that are then disposed of in accordance with local environmental regulations. Thus, the risks of environmental exposure of DMF 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. The residual amount of DMF in the final Active Pharmaceutical Ingredients (APIs) and associated intermediates is safety-limited by the ICH Q3C (Guideline for Residual Solvents). The facts above demonstrate that it would be appropriate for DMF to grant an exemption from authorization for the use of DMF 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. Use as solvent in scientific R&D and Quality Control DMF is a common solvent for chemical reactions in scientific R&D. DMF is also frequently used in routine analysis, especially for gas chromatography (GC), for analysis of residual solvents according to Pharmacopoeia Europa (EP 7.0) for headspace gas chromatography, and for UV/Vis spectroscopy because of its extremely good solubility properties shown for especially organic compounds as well as for polymers and inorganic compounds. Therefore, the use of DMF as analytical standard and for testing of residual solvents should be exempted from authorization (scientific R&D and Quality Control). Article 58(2) of REACH allows for uses to be exempted from the authorisation requirement provided that, on the basis of specific Community legislation imposing minimum requirements relating to the protection of human health or the environment, the risk is properly controlled. In the case of DMF Commission Directive 2009/161/EU has established an Indicative Occupational Exposure Limit Value (IOELV), to be transposed into national law latest 1 December 2011. The IOELV has been established based on the most recent scientific data, and sets threshold levels of exposure below which, in general, no detrimental effects are expected after short-term or daily exposure over a working life time. Hence, all possible risks posed by this substance in the workplace are already properly controlled by	

			existing specific Community legislation.	
2368	2013/09/23 04:32	Company, United Kingdom	Use exemptions should apply to: - Use applications where the volume is <100 litres per year per use where [DMF IS NOT present in the final product. - DMF used as a solvent in manufacture and dispensing of chemical dyes and other research chemical products under laboratory conditions where the final products do not contain the DMF. - DMF used in R&D and PPORD where the final chemical products are used in medical research and development by public and private organizations and pharmaceutical companies to investigate cellular disease processes, with a goal of developing more effective pharmaceuticals and therapies. - Processes using DMF meet the requirements of local national legislation COSHH. Use descriptors: o PC0 Other – UCN code O15000 Solvents o PROC3 Used in closed batch process (synthesis or formulation) o PROC15 Use as laboratory reagent o PC21 Laboratory chemicals o PC19 Intermediate o ERC4 Industrial use of processing aids in processes and products, not becoming part of articles. No release of the substance to water, air or soil. 100 % of the substance is handled as hazardous waste and treated by authorized waste vendor. o SU3 Industrial uses: Uses of substances as such or in preparations at industrial sites o SU9 Manufacture of fine chemicals - C20.5.9 Manufacture of other chemical products n.e.c. o SU24 Scientific research and development There are currently no known technically equivalent substitutes for the use of DMF in PPROD, as process chemical (i.e., solvent) in the manufacture of fine chemicals and chemicals or other research chemical products that downstream are: • Used in medical R&D by public and private institutions to investigate cellular disease processes, which is critical to development and advancement of pharmaceuticals and therapies. DMF is not part of the final fine chemical. We therefore request ECHA's consideration to exempt the use of N,N-dimethylformamide as a process chemical (solvent) in the manufacture of fine chemicals and chemical products used in medical research and development, and PPORD.	Thank you for your comment. As regards your request for exemption please note that uses (or categories of uses) can only be exempted from the authorisation requirement on the basis of Article 58(2) of REACH, unless they are already explicitly exempted in REACH Art. 2(5 or 8) or in Art. 56(3 – 6). Uses in Scientific Research and Development are exempted from authorisation as set out in Article 56(3). Article 3(23) defines SRD as "any scientific experimentation, analysis or chemical research carried out under controlled conditions in a volume less than 1 tonne per year". Note also that only substances used directly for research (or analytical purpose), whether on their own, in mixture, or in conjunction with analytical equipments, can benefit from the SRD exemption. Please see also response to comment 2456 (section I).

			There are currently no known technically equivalent substitutes for the use of DMF in PPROD, as process chemical (i.e., solvent) in the manufacture of fine chemicals and chemicals or other research chemical products that downstream are: • Used in medical R&D by public and private institutions to investigate cellular disease processes, which is critical to development and advancement of pharmaceuticals and therapies. DMF is not part of the final fine chemical. We therefore request ECHA's consideration to exempt the use of N,N-dimethylformamide as a process chemical (solvent) in the manufacture of fine chemicals and chemical products used in medical research and development, and PPORD.	
2365	2013/09/22 22:22	Company, Germany	Exemption from Authorisation for the use of N,N-Dimethylformamide (DMF) CAS 68-12-2 as a solvent in the production of Active Ingredients for Plant Protection Products since the use of DMF in manufacturing of Active Ingredients in Plant Protection Products meets the requirements set out in Article 58(2) of the REACH Regulation and on this basis should be exempt from REACH Authorization requirements	Thank you for your comment. Please see response to comment 2456 (section I) and comment 2365 (section I).
2356	2013/09/20 20:21	Company, France	We consider the use of DMF as synthesis solvent for the production of pharmaceutical ingredients should be exempted from authorization considering the ratio benefit/risk and the possibility to protect employees in the respect of French and European regulation. For instance 8h and 15 min DNEL (respectively 5 and 10 ppm) are defined as compulsory in the french Work Code.	Thank you for your comment Please see response to comment 2456 (section I).
2354	2013/09/20 19:46	Company, France	- As medical devices, under COUNCIL DIRECTIVE 93/42/EEC of 14 June 1993, with high interest for the safety of the persons, - As the use of DMF is already under control (national requirements for safety of the workers and risk for environment), We propose to exclude the process to obtain medical devices from the scope of the authorization requirements. Proposed rules Categories of uses : PROC 2, PROC 3, PROC 4 + medical devices, under COUNCIL DIRECTIVE 93/42/EEC of 14 June 1993	Thank you for your comment. Please see response to comment 2456 (section I) and comment 2414 (in this section).
2353			DMF use for a glass coating process	Thank you for your comment and the information provided.
2347	2013/09/20 18:27	Company, Ireland	Active pharmaceutical ingredient development and manufacturing uses of DMF meet the requirements set out in Article 58 (2) of REACH and on this basis should be exempted	Thank you for your comment. Please see response to comment 2456

			from REACH Authorisation requirements	(section I).
2343	2013/09/20 17:33	Individual, Italy	DMF is used as solvent producing polyurethane elastomers in solutions, destined to industrial manufacturing of synthetic leather and technical articles. The synthesis takes place in closed systems designed to prevent both emissions into the environment and exposure of workers: the incoming raw material is delivered through truck tanks and downloaded in dedicated tanks, then the solvent is pumped via pipelines inside the vessels where the chemical syntheses occur. During the whole process there is not significant exposure for humans; the workers involved in the process are correctly equipped with the personal safety disposals as described in the SDS. Every company periodically monitors and checks the level of exposure of workers. The workplace assessments show values that are much lower compared to the European IOEL. Therefore, the production processes and the prevention measures taken during processing, in accordance with Good Manufacturing Practices (GMP), allow to significantly reduce the risk of worker's exposure to DMF. These measures are identified with the installation of effective suction systems and with the handling of substances in closed systems that reduce significantly the risk of dispersion in the environment. The captured gasses are then combusted in order to destroy any residual DMF. The chemical-physical properties of DMF make it currently irreplaceable for the synthesis of polyurethane polymers. An important commitment in research has been undertaken for several years in order to identify and develop a valid substitute of DMF for industrial usage. Unfortunately at the moment it hasn't already been identified an alternative solutions with a lower hazard profile than DMF. DMF is used as solvent producing synthetic and artificial leather, synthetic fibres. DMF takes part in two different processes: PU (polyurethane resins) coating (transfer and direct) and coagulation ones. In the coating process, which is the most common in Europe, DMF is used as a solvent into the polyurethane resins. The PU is coated on the release paper (transfer coating process) or directly on the fabric (direct coating). Both coats are totally dried through tunnels (ovens – a coating line can have from 3 to 5 ovens) while in the coagulation process the textile is impregnated with polyurethane solution in DMF, coagulated with water and then completely dried.	Thank you for your comment. Please see response to comment 2456 (section I) and response to your comment in section I.

			At every step in both processes DMF solvent is entirely recovered through solvent abatement systems. In the case of the coagulation process DMF is recovered by distillation and re-used. Specifically, the fumes derived by the ovens are carried in abatement systems in order to recover both DMF and water. During the production processes many prevention measures are taken, such as: - Uses of PPE (goggles, masks, gloves, workwear, ect.); - Lev controls (Local Exasted Ventilation); - Medical reports of systematic screenings of all operators involved. Generally speaking women are not employed at work stations. If occasionally present, they are banned to stay when pregnant. All these measures allow to significantly reduce the risk of worker exposure to DMF. These measures are identified also with the installation of solvent abatement systems that significantly reduce the risk of dispersion in the environment. Every 6 months we analyze the EMISSIONS and the maximum values are around 10 mg/m3. Controls conducted by industries in the workplace demonstrated how the concentration of DMF are far below the TLV-TWA equal to 15 mg/m3, normally are around 10 mg/m3. The periodic analysis on workers, as specified above, have always confirmed the lack of exposure to DMF and the efficiency of prevention measures adopted. The processes described use all the prevention measures necessary to ensure that DMF won't be present in the finished articles. On the contrary, finished products imported from outside Europe may have a higher level of DMF, since it's not possible to control their production processes.	
2341	2013/09/20 17:24	C.O.I.M. S.p.A., Company, Italy	We agree with the position explained by Federchimica, in particular about the use of DMF as solvent producing polyurethane elastomers in solutions, destined to industrial manufacturing of synthetic leather and technical articles and as solvent producing synthetic and artifical leather	Thank you for your comment. Please see response to comment 2456 (section I).
2338	2013/09/20 16:21	Company, Netherlands	We request exemption of the use of the substance as an industrial extraction solvent in a continuous process under conditions of rigorous containment. The process involves continuous recirculation with phases of solute extraction and regeneration by separation from that solute. These conditions are equivalent to those for which exemptions are already recognized in Articles 2 (8 b) and 56 (4 c & d). The substance is used in various petrochemical facilities to extract acetylene from ethylene-rich products from a steam cracker, whose feedstock comprises other petroleum streams.	Thank you for your comment. Please see response to comments 2456, 2488 and 2427 and 2311 in section I.

			As is common in such petrochemical facilities, the materials involved in this process are handled in conditions of rigorous containment in a plant of high integrity. A solvent extraction process is used for this specific purpose as the normal distillation method for separating hydrocarbons cannot be used due to the explosive characteristics of acetylene. Due to the aprotic nature required of any solvent used to separate acetylene from ethylene, potential alternatives to the substance can be expected to share a toxicological profile. NMP (N-Methyl-2-pyrrolidone) and DMAC (N,N-Dimethylacetamid) have the same hazard profile as the substance: NMP has been proposed for restriction, DMAc and DMF for authorization. In the absence of a viable substitute solvent, the likely industry response would be investment in equipment for hydrogenation of the acetylene component in the ethylene stream (to ethylene), with consequent loss of the acetylene production to be backfilled by imports. The resulting loss of acetylene production and competitiveness of EU steam cracking operators run counter to the aim and scope of the REACH regulation recognized in Article 1 . We therefore wish to engage with ECHA to agree on the process of allowing exemption for use of the substance as industrial extraction solvent in a continuous process with rigorous containment.	
2319	2013/09/20 14:24	Sanofi-Aventis SpA, Company, Italy	Legal Entity X is part of the Sanofi Holding a member of the ChemLeg Pharmaceutical Companies network which wrote a collective comment to the public consultation on the incorporation of DMF into the REACh Annex XIV. This comment is attached hereafter and has also been addressed to ECHA by the European Federation of Pharmaceutical Industries and Association	Thank you for your comment. Please see response to comment 2456 (section I).
2318	2013/09/20 14:21	Sanofi Chimie, Company, France	Legal Entity X is part of the Sanofi Holding a member of the ChemLeg Pharmaceutical Companies network which wrote a collective comment to the public consultation on the incorporation of DMF into the REACh Annex XIV. This comment is attached hereafter and has also been addressed to ECHA by the European Federation of Pharmaceutical Industries and Association	Thank you for your comment. Please see response to comment 2456 (section I).
2312	2013/09/20 12:57	CHINOIN Private Co. Ltd., Company, Hungary	The use of DMF in the manufacturing of pharmaceutical 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 is	Thank you for your comment. Please see response to comment 2456 (section I).

			exempted from REACH authorisation requirements. This exemption would also include all PPORD uses of DMF (up to 50ts/pa) in the production of medicinal and veterinary products. Rationale for the Request for an Exemption as per Art 58(2) As we are all aware, a directive is a legal instrument provided for in the EU Treaty and to date the majority of Community HSE legislation is based on the choice of the directive as the most appropriate legal instrument. It is binding in its entirety and obliges Member States to transpose it into national law within the deadlines clearly set out in the directive. A directive enters into force once it is published in the Official Journal of the EU. EU directives on safety and health at work have their legal foundation in Article 153 of the Treaty on the Functioning of the European Union (ex Article 137 TEC), which gives the EU the authority to adopt directives in this field. A wide variety of EU directives setting out minimum health and safety requirements for the protection of workers have since been adopted. Member States are free to adopt stricter (but not less strict) rules for the protection of workers when transposing EU directives into national law, and so legislative requirements in the field of safety and health at work can vary across EU Member States. The decision to recommend DMF for inclusion in Annex XIV is based solely on occupational health risks (DMF is classified as toxic for reproduction category 1b). Those risks are already properly controlled (as outlined below) by the application of Directive 98/24/EC (Chemical Agents Directive), Directive 2009/161/EU (IOEL for DMF), Directive 92/85/EC (Pregnant Workers), Directive 2010/75/EU (Industrial Emissions Directive) and 2001/83/EC (Medicinal Products Directive) which impose minimum requirements that must be transposed into national legislation by EU Member States (quotations from legislation is given below in italics) 98/24/EC Chemical Agents Directive (CAD) Article 1 of Directive 98/24/EC This Directive ..... lays down minimum requirements for the protection of workers from risks to their safety and health arising, or likely to arise, from the effects of chemical agents that are present at the workplace or as a result of any work activity involving chemical agents. Article 6(2) of Directive 98/24/EC Substitution shall by preference be undertaken, whereby the employer shall avoid the use of a hazardous chemical agent by replacing it with a chemical agent or process which, under its condition of use, is not hazardous or less hazardous to workers'	

			safety and health, as the case may be. Where the nature of the activity does not permit risk to be eliminated by substitution, having regard to the activity and risk assessment referred to in Article 4, the employer shall ensure that the risk is reduced to a minimum by application of protection and prevention measures, consistent with the assessment of the risk made pursuant to Article 4. These will include, in order of priority: • Design of appropriate work processes and engineering controls and use of adequate equipment and materials, so as to avoid or minimise the release of hazardous chemical agents which may present a risk to workers' safety and health at the place of work; • Application of collective protection measures at the source of the risk, such as adequate ventilation and appropriate organizational measures; Where exposure cannot be prevented by other means, application of individual protection measures including personal protective equipment. 1. We believe ECHAs previous interpretation of the minimum requirements as outlined in CAD is contrary to the principles of proportionality. The legal obligation on the employer to put in place specific protection and prevention measures is in keeping with the principles of proportionality. A technical feasibility assessment of control measures beyond what is recommended by a chemical agents risk assessment is disproportionate. Note the clear intentions of CAD: "To ensure not only the protection of the health and safety of each individual worker but also to provide a level of minimum protection of all workers in the Community which avoids any possible distortion in the area of competition" (Preamble 4 of Directive 98/24/EC) 2009/161/EU Indicative OEL Values Directive Article 2 of Directive 2009/161/EU Member States shall establish national occupational exposure limit values for the chemical agents listed in the Annex, taking into account the Community values. 1. 98/24/EC (CAD) requires setting of indicative occupational exposure limit values (IOELVs) in all Member States (who are obligated to do transpose this and that their national limits must, at a minimum, be as stringent as the EU levels). DMF is referenced in Directive 2009/161/EU, establishing a third list of indicative occupational exposure limit values in implementation of Council Directive 98/24/EC and amending	

			Commission Directive 2000/39/EC The following OEL has been set for DMF within EU law: 8 hour TWA: 5 ppm (15mg/m³), STEL (15 mins): 10 ppm (30mg/m³). Austria, Belgium, France, Germany, Ireland, Italy, Netherlands and UK are, to name but a few, Member States that have transposed this OEL into their National Legislation. ChemLeg members across various EU Member States have actual DMF monitoring data that can be shared with ECHA to show the controls used within our manufacturing facilities enables us to comply with the DMF OEL. 2. Furthermore, "A registrant is allowed to use an IOEL as a DNEL for the same exposure route and duration, unless new scientific information that he has obtained in fulfilling his obligations under REACH does not support the use of the IOEL for this purpose." [ ]. According to the ECHA guidance, IOEL values are valid DNELs to be accepted for occupational uses. If the CMR properties were considered when deriving the IOEL, there is no scientific reason for ECHA not to accept the IOEL unless new experimental data has been generated. In Summary: DMF is referenced in 2009/161/EU and has been given a minimum OEL. Therefore 2009/161/EU should satisfy Art 58(2) Existing Community Legislation. Not accepting this Directive as satisfying the requirements for an exemption under Article 58(2) undermines the legal authority of Directive 2009/161/EU and creates a situation of double regulation which is against the principle of the EU Commission's approach to "Smart Regulation". ChemLeg members have data to show existing OEL for DMF is complied with at API Manufacturing facilities across various Member States. 92/85/EC Pregnant Workers, Recently Given Birth or Breast Feeding Article 5 • If the results of the assessment referred to in Article 4 (1) reveal a risk to the safety or health or an effect on the pregnancy or breastfeeding of a worker within the meaning of Article 2, the employer shall take the necessary measures to ensure that, by temporarily adjusting the working conditions and/or the working hours of the worker concerned, the exposure of that worker to such risks is avoided. • If the adjustment of her working conditions and/or working hours is not technically and/or objectively feasible, or cannot reasonably be required on duly substantiated grounds,	

			the employer shall take the necessary measures to move the worker concerned to another job. • If moving her to another job is not technically and/or objectively feasible or cannot reasonably be required on duly substantiated grounds, the worker concerned shall be granted leave in accordance with national legislation and/or national practice for the whole of the period necessary to protect her safety or health. • The provisions of this Article shall apply mutatis mutandis to the case where a worker pursuing an activity which is forbidden pursuant to Article 6 becomes pregnant or starts breastfeeding and informs her employer thereof. 1. Directive 92/85 provides for the necessary measures to be taken by the employer in case of risk or effect on the pregnancy or breastfeeding of a worker In Summary: Some active pharmaceutical ingredients by the very nature of their pharmacological action are Reprotoxins e.g. antimitotic drugs. Bulk API plants handling these substances (such as DMF) typically have reproductive hazard evaluation programmes in place covering APIs and solvents to protect the employee planning a pregnancy or recently become pregnant. Examples of risk reduction recommendations include additional PPE, delegating tasks to non-pregnant employees or banning such workers entering areas where DMF type substances are handled. Therefore 92/85/EC should satisfy Art 58(2) Existing Community Legislation 2010/75/EU Industrial Emissions Directive IED Art 58: Substitution of Hazardous Substances Substances or mixtures which, because of their content of volatile organic compounds classified as carcinogens, mutagens, or toxic to reproduction under Regulation (EC) No 1272/2008, are assigned or need to carry the hazard statements H340, H350, H350i, H360D or H360F, shall be replaced, as far as possible by less harmful substances or mixtures within the shortest possible time IED Art 59(5) Control of Emissions: The emissions of either volatile organic compounds which are assigned or need to carry the hazard statements H340, H350, H350i, H360D or H360F or halogenated volatile organic compounds which are assigned or need to carry the hazard statementsH341 or H351, 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 set out in Part 4 of Annex VII . 1. DMF is used in Bulk Pharma manufacturing facilities to manufacture API; all Bulk Pharma API manufacturing facilities are required to have a PPC Permit (soon to be Industrial Emissions Permit under the Industrial Emissions Directive). This requirement is referenced in Annex I of the IED (section 4.5). 2. The IED (and the previous directives that have now been included within it including 2000/76/EC) requires permit holders who use H360D compounds to replace them, as far as possible, by less harmful substances within the shortest period of time. DMF is a H360D substance 3. The IED requires permit holders that emissions of H360D substances shall be controlled under contained conditions as far as technically and economically feasible to safeguard public health and the environment. DMF is a H360D substance. 4. DMF used in the API manufacturing stage is collected after use and (in the majority of cases) is incinerated (under the Waste Incineration Directive 2000/76/EC soon to be incorporated into the Industrial Emissions Directive). Where DMF is not incinerated, it is recycled. In Summary: All bulk API facilities using DMF must have an Industrial Permit to operate. That permit lays down minimum conditions to protect the environment as well as requiring substitution of H360D substances. The EU Commission does not need to implement further legislation to require the substitution of H360D substances (that are used in an IED permitted facility). All waste DMF is handled appropriately. Community Legislation (2010/75/EU) properly controls the emissions of DMF associated with the manufacture of APIs and the use of the API during drug manufacture. Therefore 2010/75/EU should satisfy Art 58(2) Existing Community Legislation 2010/75/EU Industrial Emissions Directive (Solvents) IED Annex VII Technical Provisions relating to Installations and Activities using Organic Solvents Part 1(Activities): (8). Manufacturing of pharmaceutical products: The chemical synthesis, fermentation, extraction, formulation and finishing of pharmaceutical products and, where carried out at the same site, the manufacture of intermediate products IED Annex VII Technical Provisions relating to Installations and Activities using Organic Solvents Part 2(Thresholds and Emission Limit Values): (20). Manufacturing of pharmaceutical	

			products: >50ts/yr. of solvents; waste gases emission limit 20mg/m³; total ELV is 15% of solvent output IED Art 59(1) Control of Emissions: Member States shall take the necessary measures to ensure that each installation complies with either of the following: (a) the emission of volatile organic compounds from installations shall not exceed the emission limit values in waste gases and the fugitive emission limit values, or the total emission limit values, and other requirements laid down in Parts 2 and 3 of Annex VII are complied with Existing Community Legislation (2010/75/EU) properly controls the emissions of DMF associated with the manufacture of APIs and the permitting/use/storage of the solvent during drug manufacture. One objective of the IED is to prevent or reduce the direct and indirect effects of emissions of VOCs during the manufacture of pharmaceutical products into the environment, mainly into air, and the potential risks to human health, by providing measures and procedures to be implemented for certain activities. The IED already governs and manage the risks that the inclusion of Pharma uses of DMF in REACH Annex XIV seeks to manage. Article 62 (5b) of the REACH Regulation would suggest that this is also the case. In Summary: All bulk API facilities using >50ts/yr. of solvents (including DMF) must have an Industrial Permit to operate. That permit lays down maximum emission to air limits for solvents, therefore the IED provides minimum emission to air standards in API Bulk Manufacturing facilities using >50ts/yr. of solvents. This shows that DMF is properly controlled. Therefore 2010/75/EU should satisfy Art 58(2) Existing Community Legislation Medicinal Products Directive: Directive 2001/83/EC & Regulation (EC) No 726/2004 1. The EU medicinal regulatory system protects public health and secures the availability of medicinal products for EU citizens by requiring all such products to have been granted a Marketing Authorisation (MA) of before they are placed on the EU market. These MAs are granted only if the manufacturing process complies with the EU quality standards known as "good manufacturing practices." After a MA is issued, MA holders may not introduce any changes into the manufacturing process without the consent of the Member State competent authority. Finally, once a medicinal product has been authorised and placed on the EU market, its safety is monitored throughout its	

			entire lifespan to ensure that, in case of adverse reactions that present an unacceptable level of risk under normal conditions of use, it is rapidly withdrawn from the market. This is done through the EU system of "Pharmacovigilance" set out in the Medicinal Products Directive (MPD). 2. We believe that the MPD does properly control the risks of the use of DMF within the manufacture of an API that 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 MA of a medicinal product referred to in Article 40 of Directive 2001/83/EC is obliged "to comply with the principles and guidelines of good manufacturing practice (GMP)" as laid down by community law. Principles and guidelines of GMP require impurity testing of pharmaceutical ingredients to ensure that specific threshold limits for residual solvents are met. All Pharmaceutical products that are impacted by such solvents have the information included in the MA which can be withdrawn if the pharmaceutical product does not meet the residual solvent specification. This concentration limit is enforced via the Member State relevant Health Regulator (e.g. MHRA in the UK). EMA guidance on residual solvents (EMA/CHMP/ICH/82260/2006) contains specific limits for DMF (PDE 8.8mg/day and 880ppm). 3. Since the residual amount of DMF in the eventual pharmaceutical product is safety-limited by the EMA (Guideline for Residual Solvents in practice virtually all the DMF used during manufacture of the API would be present in the waste streams that are then disposed of via incineration as hazardous waste (under the Waste Incineration Directive 2000/76/EC soon to be incorporated into the Industrial Emissions Directive). Where DMF is not incinerated, it would be purified and recycled into DMF that can be used again. 4. Recital 111 of REACH cautions against mixing the policy aims of REACH with the policy aims of the European Medicines Agency (EMA). The legislative history of REACH reflects the special relationship between the chemical and medicinal regulatory regimes. The Commission expressly addressed the interaction between the two regimes when it proposed REACH, indicating how it would avoid potential overlaps (thereby showing that the Commission was (i) aware of the potential overlap between REACH and the medicines legislation and (ii) it aimed to avoid such overlap): "Certain uses of substances are not subject to authorisation because their human health and environmental effects are	

			considered to be addressed by equivalent Community legislation. It would be unreasonable to subject such uses to two systems with the cost and resources this would imply. The Commission will propose a modification of the legislation on medicinal products for human use and veterinary use respectively to address risks related to the environment. This will be part of the benefit/risk assessment which has to be positive as a prerequisite for approval of the medicinal product". [Emphasis added] In Summary: Firstly, the REACH Regulation was not meant to overlap with or impede the functioning of this Medicinal regulatory regime. Indeed, substances used in medicinal products for human and veterinary use and falling under the scope of the Medicinal Products Legislation are specifically exempted from the REACH authorisation requirements. Secondly, in line with the text of REACH, the history of the Regulation, and the proportionality principle, we believe that ECHA should avoid any conflict with the EMA's specific authority to approve the market placement of medicinal products. Thirdly, 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). Therefore 2001/83/EC and its associated Guidance should also help satisfy our compliance with the conditions for exemption set down in Art 58(2) with regard to existing Community Legislation. Conclusions: • In the comments above, we have cited various EU laws which, collectively and individually, meet the conditions imposed for the exemption under Article 58.2 of REACh • 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, not only by REACh 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… • Pharmaceutical manufacturing uses of DMF meet the requirements set out in Article 58 (2) of REACH and on this basis, should be exempted from REACH Authorisation requirements; • Our uses of DMF as an aprotic solvent are already governed by existing EU legislation setting minimum requirements for the proper control of risks to human health or the environment; • There will be no direct or net environmental benefit by including Pharma uses of DMF in Annex XIV; • Use of DMF in pharmaceutical manufacturing is not widely dispersive, and the scoring system applied in Annex XV would not qualify DMF as used in Pharma for prioritization • REACH article 62(5)(b)(i) suggests that an Annex XIV listed substance handled in a facility that is permitted by Directive 96/61/EC (soon to be incorporated into 2010/75/EU IED) doesn't need to consider risks from Human Health or the Environment when submitting an application for an Authorised Use of that Substance. This therefore exempts annex XIV listed substances from Authorisation if the substance is used in an IPPC Permitted facility and no economic or technically feasible substitution substances exist NOTE: DMF belongs to a class of "aprotic solvents" which also includes the solvent N,N-dimethylacetamide (DMAC). It should be noted that the proposed listing of DMAC on Annex XIV is currently subject to discussions between representatives of the pharmaceutical industry and the authorities, both on CA level in the Member States and on EC level. The arguments provided on DMAC from the EU Pharma ChemLeg Group are similar to the ones discussed in this consultation response.	
2307	2013/09/20 12:13	SABIC Petrochemical s B.V., Industry or trade association, Netherlands	In case authorization would still be pursued, SABIC proposes to exempt the use of DMF as extraction agent for acetylene and butadiene in steam cracking and related butadiene production. These uses are already in line with directive 2009/161/EU (17.12.2009), regulating the setting of national exposure limits, and also with directive 98/24/EC (Protection of health and safety of workers from risks related to chemical agents at work) and Directive 96/61 (VOC directive). Thus the uses as such should be exempt from authorisation under REACH Article 62 (5b).	Thank you for your comment. Please see response to comment 2456 (section I).

2298	2013/09/20 11:06	Assogastecnici/Federchimica, Industry or trade association, Italy	Assogastecnici requests to exempt from the authorisation process "the use of DMF as a solvent and stabilizer for acetylene in bundles of gas cylinders, in multiple elements gas containers (MEGC) and in battery-vehicles" for the following reasons: 1. There is already existing EU legislation that adequately protects those exposed: there are established IOELV values of 5ppm/15mg/m3. From Assogastecnici experience the exposure of workers to DMF is much lower than the IOELV. Furthermore the exposure to DMF happens only during the legally required 10 yearly retest which takes a very small amount of time in which acetylene gas cylinder are opened. 2. Any DMF withdrawn with the acetylene is burnt in the process of the final user of the acetylene. 3. The use of DMF in bundles of cylinders, MEGC and battery-vehicles is safer than the only presently approved available alternative, that is acetone, because of two different reasons: 3.1. it drastically reduces the need of disassembling the equipment for the make-up of the lost solvent, thus minimizing the risk of acetylene leakages (flammable and chemically unstable gas) from connections after reassembling operations. 3.2. acetylene is stabilised in the single cylinder by means of porous material and a solvent in which this gas is dissolved. Should the amount of solvent be less than required, the pressure receptacle cannot be considered safe because of the risk of explosion or chemical decomposition. DMF has a much lower vapour pressure than acetone and for this reason, especially for high gas flow rates, the solvent carry-over is not significant and does not lead to "solvent depletion". On the strategy to manage the risks of DMF: Assogastecnici thinks that the risks of DMF should be better managed by the restriction process considering that the use in industrial settings is adequately protected by existing legislation and that the use by consumers is forbidden.	Thank you for your comment. Please see response to comment 2456 and 2427 in section I.
2295	2013/09/20 10:40	Federchimica, Industry or trade association, Italy	1) DMF is used as solvent producing polyurethane elastomers in solutions, destined to industrial manufacturing of synthetic leather and technical articles. The synthesis takes place in closed systems designed to prevent both emissions into the environment and exposure of workers: the incoming raw material is delivered through truck tanks and downloaded in dedicated tanks, then the solvent is pumped via pipelines inside the vessels where the chemical	Thank you for your comment. Please see response to comment 2456 (section I).

			syntheses occur. During the whole process there is not significant exposure for humans; the workers involved in the process are correctly equipped with the personal safety disposals as described in the SDS. Every company periodically monitors and checks the level of exposure of workers. The workplace assessments show values that are much lower compared to the European IOEL. Therefore, the production processes and the prevention measures taken during processing, in accordance with Good Manufacturing Practices (GMP), allow to significantly reduce the risk of worker's exposure to DMF. These measures are identified with the installation of effective suction systems and with the handling of substances in closed systems that reduce significantly the risk of dispersion in the environment. The captured gasses are then combusted in order to destroy any residual DMF. The chemical-physical properties of DMF make it currently irreplaceable for the synthesis of polyurethane polymers. An important commitment in research has been undertaken for several years in order to identify and develop a valid substitute of DMF for industrial usage. Unfortunately at the moment it hasn't already been identified an alternative solutions with a lower hazard profile than DMF. 2) DMF is used as solvent producing synthetic and artificial leather, synthetic fibres. DMF takes part in two different processes: PU (polyurethane resins) coating (transfer and direct) and coagulation ones. In the coating process, which is the most common in Europe, DMF is used as a solvent into the polyurethane resins. The PU is coated on the release paper (transfer coating process) or directly on the fabric (direct coating). Both coats are totally dried through tunnels (ovens – a coating line can have from 3 to 5 ovens) while in the coagulation process the textile is impregnates with water and a polyurethane resin and then completely dried. At every step in both processes DMF solvent is entirely recovered through solvent abatement systems. In the case of the coagulation process DMF is recovered by distillation and re-used. Specifically, the fumes derived by the ovens are carried in abatement systems in order to recover both DMF and water. During the production processes many prevention measures are taken, such as: - Uses of PPE (goggles, masks, gloves, workwear, ect.); - Lev controls (Local Exasted Ventilation);	

			- Medical reports of systematic screenings of all operators involved. Generally speaking women are not employed at work stations. If occasionally present, they are banned to stay when pregnant. All these measures allow to significantly reduce the risk of worker exposure to DMF. These measures are identified also with the installation of solvent abatement systems that significantly reduce the risk of dispersion in the environment. Controls conducted by industries in the workplace demonstrated how the concentration of DMF are far below the TLV-TWA equal to 15 mg/m3. The periodic analysis on workers, as specified above, have always confirmed the lack of exposure to DMF and the efficiency of prevention measures adopted. The processes described use all the prevention measures necessary to ensure that DMF won't be present in the finished articles. On the contrary, finished products imported from outside Europe may have a higher level of DMF, since it's not possible to control their production processes. 3) DMF is used as solvent for the production of intermediates that are then used to obtain: - medicinal products; - biocides; - fine chemicals. The use of DMF for the production of intermediates for the synthesis of APIs (pharmaceutical industry) is performed within enclosed equipment in accordance with Good Manufacturing Practices (GMP), with respect of the intermediates used in the fine chemicals and or for the production of Active Biocidal, in agreement with the REACH Regulation, the intermediates are obtained and used (transformed) under strictly controlled conditions in that it is rigorously contained by technical means during its whole lifecycle. For these reasons, in all the three fields of application mentioned above the DMF is introduced into the reactors via transfer systems designed to minimize environmental release, by trained personnel, and is thus contained within the process stream. In practice all the DMF used during manufacture (in closed systems) is captured in waste streams which are typically combusted under strictly controlled conditions in order to destroy all residual DMF. Controls conducted by industries in the workplace demonstrate how the concentrations of DMF are far below the TLV-TWA equal to 15 mg/m3. Periodic analysis on workers confirm the lack of exposure to DMF and the efficiency of prevention	

			measures adopted. The use of DMF to produce medicinal products, biocides and fine chemicals works similarly. Using the first category as an example, we see that DMF is mostly used as polar aprotic solvent (e.g. nucleophilic substitution) in the synthesis of active pharmaceutical ingredients (APIs) and associated intermediates. DMF offers generally high solubility of many APIs and intermediates and sufficient solubility of many inorganic reagents (e.g. acids and bases). Furthermore, DMF has a high boiling point (153oC), low vapor pressure, and is soluble in water. Because of these characteristics DMF is an essential and highly specific solvent within the processes used by pharmaceutical and biopharmaceutical industries. 4) DMF is used as solvent and stabilizer for acetylene in bundles of gas cylinder, in multiple elements gas containers (MEGC) and in battery-vehicles. Only two solvents are authorized to be used in the acetylene pressure receptacles: acetone and DMF. The use of DMF in bundles of cylinders, MEGC and battery-vehicles is safer than the only presently approved available alternate, acetone, for two reasons: • the much lower vapour pressure allows to minimize the solvent depletion of the cylinder, thus ensuring that even in high gas flow applications, the cylinders are safe; • it eliminates the need to regularly and frequently disassemble the equipment for the make-up of the lost solvent required for safe transport of acetylene. The reduction of assembling/disassembling operations minimizes the risk of leakages from interconnecting piping on board of bundles, MEGC, battery-vehicles. The risk of exposure for DMF in the industrial gases industry is limited as the DMF is inside the cylinder as a solvent used for stabilization of the acetylene and not as a product that is consumed. The DMF is introduced when the cylinder is first manufactured or when the solvent content of the cylinder is below a minimum safe level (which happens only very seldom, in case of DMF). When DMF is introduced into the cylinder, this operation is carried out in closed system under local ventilation, so that exposure for the operator is negligible. In addition, every ten years under European legislation there is a requirement to visually inspect the porous material which is inside the acetylene cylinders. These two are the only occasions when an operator could be	

			exposed to DMF. Concerning the exposure of the acetylene users, it shall be taken into account that acetylene is burnt in a flame to create a cutting torch. The DMF (also flammable) is consumed (and therefore destroyed) in the flame. Therefore the normal use of acetylene presents a negligible risk of exposure to the DMF. Conclusion: According to Article 58(2) are to be considered the exemptions for categories of uses listed above because there is already existing Community legislation that imposes minimum requirements to control the risks connected to the use of DMF. About reprotoxic substances like DMF, specific measures to ensure safe use are already provided in Council Directive 98/24/EC (Protection of health and safety of workers from risks related to chemical agents at work) and Council Directive 92/85/EEC (Measures to encourage improvements in the safety and health at work of pregnant workers and workers who recently given birth or are breastfeeding). Furthermore, there is a restriction in REACH (annex XVII, entry 30) for substances classified as reprotoxic cat. 1 and cat.2. Also, VOC-Directive 1999/13/EC gives requirements already met by industries in work processes, so Authorization dossier will not add other added values to prevent risks to human health and environment. DMF is included in the third list of indicative occupational exposure limit values (IOEL) established by Commission Directive 2009/161/EU of 17 December 2009 (TLV-TWA: 15 mg/m3, 5 ppm; TLV-STEL: 30 mg/m3; 10 ppm). According to the ECHA guidance, IOEL values are valid DNELs to be accepted for occupational uses. If the CMR properties were considered when deriving the IOEL there is no scientific reason for ECHA not to accept the IOEL unless new experimentally data has been generated. The fact that a substance is an SVHC candidate or recommended for authorization is not new scientific information with respect to health effect. In addition, the prevention measures taken during DMF processing include periodical and continual monitoring on workers through: - analysis of the concentrations of a chemical marker in a human biological media - Biological Exposure Index (BEI); - analysis of a substance’s concentration in the ambient air in the workplace (indoor air quality); - inhalation exposure of workers (TLV-TWA and TLV-	

			STEL values). All the values obtained where always below the limits indicated by Community legislation. In conclusion, DMF is not intended for consumer or professional use but only for industrial use. All the industrial uses described above, properly control the risks connected to human health and the environment.	
2286	2013/09/19 20:35	Company, Ireland	The use of DMF in the manufacturing of pharmaceutical 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 is exempted from REACH authorisation requirements. This exemption would also include all PPORD uses of DMF (up to 50ts/pa) in the production of medicinal and veterinary products. A directive is a legal instrument provided for in the EU Treaty and to date the majority of Community HSE legislation is based on the choice of the directive as the most appropriate legal instrument. It is binding in its entirety and obliges Member States to transpose it into national law within the deadlines clearly set out in the directive. A directive enters into force once it is published in the Official Journal of the EU. EU directives on safety and health at work have their legal foundation in Article 153 of the Treaty on the Functioning of the European Union (ex Article 137 TEC), which gives the EU the authority to adopt directives in this field. A wide variety of EU directives setting out minimum health and safety requirements for the protection of workers have since been adopted. Member States are free to adopt stricter (but not less strict) rules for the protection of workers when transposing EU directives into national law, and so legislative requirements in the field of safety and health at work can vary across EU Member States. The decision to recommend DMF for inclusion in Annex XIV is based solely on occupational health risks (DMF is classified as toxic for reproduction category 1b). Those risks are already properly controlled (as outlined below) by the application of Directive 98/24/EC (Chemical Agents Directive), Directive 2009/161/EU (IOEL for DMF), Directive 92/85/EC (Pregnant Workers), Directive 2010/75/EU (Industrial Emissions Directive) and 2001/83/EC (Medicinal Products Directive) which impose minimum requirements that must be transposed into national legislation by EU Member States.	Thank you for your comment. Please see response to comment 2456 (section I).
2285	2013/09/19	Individual, France	Diagnostica Stago wishes to comment on public consultation relating to a product made with DMF. See attachment	Thank you for your comment.

	19:45		confidential document.	Please refer to response to your comment in section I.
2284	2013/09/19 19:31	Individual, France	Diagnostica Stago wishes to comment on public consultation relating to DMF. See attached confidential document.	Thank you for your comment. Please refer to response to comment 2285 in section I.
2276	2013/09/19 17:29	Company, Germany	The decision to recommend DMF for inclusion in Annex XIV is based solely on occupational health risks (DMF is classified as toxic for reproduction category 1b). Those risks are already properly controlled (as outlined below) by the application of Directive 98/24/EC (Chemical Agents Directive), Directive 2009/161/EU (IOEL for DMF) and Directive 92/85/EC (Pregnant Workers) which impose minimum requirements that must be transposed into national legislation by EU Member States. Therefore, all uses conducted under those Directives should be exempted from the requirement of authorisation. 98/24/EC Chemical Agents Directive (CAD) Article 1 This Directive lays down minimum requirements for the protection of workers from risks to their safety and health arising, or likely to arise, from the effects of chemical agents that are present at the workplace or as a result of any work activity involving chemical agents. Article 6(2) Substitution shall by preference be undertaken, whereby the employer shall avoid the use of a hazardous chemical agent by replacing it with a chemical agent or process which, under its condition of use, is not hazardous or less hazardous to workers' safety and health, as the case may be. Where the nature of the activity does not permit risk to be eliminated by substitution, having regard to the activity and risk assessment referred to in Article 4, the employer shall ensure that the risk is reduced to a minimum by application of protection and prevention measures, consistent with the assessment of the risk made pursuant to Article 4. These will include, in order of priority: • Design of appropriate work processes and engineering controls and use of adequate equipment and materials, so as to avoid or minimise the release of hazardous chemical agents which may present a risk to workers' safety and health at the place of work; • Application of collective protection measures at the source of the risk, such as adequate ventilation and appropriate organizational measures; Where exposure cannot be prevented by other means,	Thank you for your comment. Please see response to comment 2456 (section I).

			application of individual protection measures including personal protective equipment. 1. We believe ECHAs previous interpretation of the minimum requirements as outlined in CAD is contrary to the principles of proportionality. The legal obligation on the employer to put in place specific protection and prevention measures is in keeping with the principles of proportionality. A technical feasibility assessment of control measures beyond what is recommended by a chemical agents risk assessment is disproportionate. Note the clear intentions of CAD: "To ensure not only the protection of the health and safety of each individual worker but also to provide a level of minimum protection of all workers in the Community which avoids any possible distortion in the area of competition" (Preamble 4 of Directive 98/24/EC) 2009/161/EU Indicative OEL Values Directive Article 2 Member States shall establish national occupational exposure limit values for the chemical agents listed in the Annex, taking into account the Community values. 1. 98/24/EC (CAD) requires setting of indicative occupational exposure limit values (IOELVs) in all Member States (who are obligated to do transpose this and that their national limits must, at a minimum, be as stringent as the EU levels). DMF is referenced in Directive 2009/161/EU, establishing a third list of indicative occupational exposure limit values in implementation of Council Directive 98/24/EC and amending Commission Directive 2000/39/EC The following OEL has been set for DMF within EU law: 8 hour TWA: 5 ppm (15mg/m³), STEL (15 mins): 10 ppm (30mg/m³). Austria, Belgium, France, Germany, Ireland, Italy, Netherlands and UK are, to name but a few, Member States that have transposed this OEL into their National Legislation. 2. Furthermore, "A registrant is allowed to use an IOEL as a DNEL for the same exposure route and duration, unless new scientific information that he has obtained in fulfilling his obligations under REACH does not support the use of the IOEL for this purpose." [ ]. According to the ECHA guidance, IOEL values are valid DNELs to be accepted for occupational uses. If the CMR properties were considered when deriving the IOEL, there is no scientific reason for ECHA not to accept the IOEL unless new experimental data has been generated. In Summary:	

			DMF is referenced in 2009/161/EU and has been given a minimum OEL. Therefore 2009/161/EU should satisfy Art 58(2) Existing Community Legislation. Not accepting this Directive as satisfying the requirements for an exemption under Article 58(2) undermines the legal authority of Directive 2009/161/EU and creates a situation of double regulation which is against the principle of the EU Commission's approach to "Smart Regulation". 92/85/EC Pregnant Workers, Recently Given Birth or Breast Feeding Article 5 • If the results of the assessment referred to in Article 4 (1) reveal a risk to the safety or health or an effect on the pregnancy or breastfeeding of a worker within the meaning of Article 2, the employer shall take the necessary measures to ensure that, by temporarily adjusting the working conditions and/or the working hours of the worker concerned, the exposure of that worker to such risks is avoided. • If the adjustment of her working conditions and/or working hours is not technically and/or objectively feasible, or cannot reasonably be required on duly substantiated grounds, the employer shall take the necessary measures to move the worker concerned to another job. • If moving her to another job is not technically and/or objectively feasible or cannot reasonably be required on duly substantiated grounds, the worker concerned shall be granted leave in accordance with national legislation and/or national practice for the whole of the period necessary to protect her safety or health. • The provisions of this Article shall apply mutatis mutandis to the case where a worker pursuing an activity which is forbidden pursuant to Article 6 becomes pregnant or starts breastfeeding and informs her employer thereof. Directive 92/85 provides for the necessary measures to be taken by the employer in case of risk or effect on the pregnancy or breastfeeding of a worker Use in synthesis Dimethylformamide (DMF) is a frequently used and important solvent for the production of various organic substances and is of special importance for the manufacture of Active Pharmaceutical Ingredients (API) or excipients. Occupational exposure is controlled through compliance with the Chemical Agents Directive (98/24/EC) on the protection of the health and safety of workers from the risks related to chemical agents at	

			work. The residual amount of DMF in the final APIs or excipients is limited by the ICH Q3C (Guideline for Residual Solvents, European Medicines Agency). Indicative occupational exposure limit values (IOELVs) for DMF are set by Commission Directive 2009/161/EU in implementing Council Directive 98/24/EC and amending Commission Directive 2000/39/EC. These levels are then used by Member States to establish their own national limits. The following safe limits have been set within EU law; 8 hour TWA: 5 ppm (15 mg/m³), STEL (15 mins): 10 ppm (30 mg/m³). Alternatives to DMF like other aprotic solvents are no real alternatives because they show the same health hazard as DMF. Use in scientific R&D DMF is a common solvent for chemical reactions in scientific R&D. In biochemistry, DMF is e.g. used for the coupling of amino acids during the peptide synthesis. DMF is used in routine analysis (scientific R&D), especially for gaschromatography (GC) and for UV/Vis spectroscopy because it is a good solvent for many substances, including polymers and inorganic compounds. DMF is used for analysis of residual solvents according to Ph Eur 7.7 (chapter 2.4.24) for headspace gaschromatography. Additionally, the substance is classified as class 2 residual solvent (Solvents that should be limited in pharmaceutical products because of their inherent toxicity, see ICH Q3C Guideline for residual solvents) in pharmaceutical synthesis. All formulations mentioned in the uses described above are used in the laboratory by industrial and professional users that are well-trained. Therefore, the use of DMF as analytical standard and for testing of residual solvents should be exempted from authorisation (scientific R&D) as well as the formulation of mixtures for R&D purpose and packaging/refilling of the pure substance and mixtures into small packages for this use in order to avoid handling of big volumes in laboratories.	
2273	2013/09/19 16:05	EURATEX, Industry or trade association, Belgium	The coating processes in the textile sector. details and justification are given is the attached file under section IV.	Thank you for your comment. Please see response to your comment in section I.
2246	2013/09/18 16:38	The Linde Group, Region Central and Northern Europe, Company, Germany	EIGA requests that "the use of DMF as a solvent and stabilizer for acetylene in bundles of gas cylinders, in multiple elements gas containers (MEGC) and in battery-vehicles" should be exempted from the authorisation process for the following reasons:	Thank you for your comment. Please see response to comment 2456 and 2427 in section I.

			1. There is already existing EU legislation that adequately protects those exposed. 1.1. DMF contained in the acetylene distribution equipment is used in industrial settings where the risk is properly controlled by the implementation of the Community legislation on the protection of workers; namely the Chemical Agents Directive 98/24/EC (CAD). 1.2. That versus the risk causing DMF to be considered for SVHC there is directive 92/85/EEC on the protection of pregnant workers. For information all workers in EIGA retest facilities are male. 1.3. That there is established IOELV values, see directive 2009/161/EU. This defines an IOELV of 5ppm/15mg/m3. The workplace assessment of the exposure to DMF at EIGA members has shown that the exposure of workers is much lower than the IOELV. Furthermore due to the small amount of time in which acetylene gas cylinder are opened for the legally required 10 yearly retest, the average worker exposure is estimated to be less than 20 hours a year. 2. Any DMF contained as impurity in the acetylene flow coming out of the distribution equipment is burnt (destroyed) with the acetylene in the process of the final user of the acetylene. 3. That the use of DMF in bundles of cylinders, MEGC and battery-vehicles is safer than the only presently approved available alternate, acetone, because it eliminates the need to regularly and frequently disassemble the equipment for the make-up of the lost solvent required for safe transport of acetylene. This is a function of DMF's inherent physical property, much lower vapour pressure (described in the ECHA dossier on the properties of substance). Notes 1. Definitions and illustrations of "bundle of cylinders", MEGC and battery-vehicle is in the attachment. 2. The descriptions of the processes to retest cylinders and the survey of the exposure during these processes are in the attachment (Section 4). On the strategy to manage the risks of DMF: Considering that the use in industrial settings is adequately protected by existing legislation and that the use by consumers is forbidden, EIGA supports the comment made to the Annex XV dossier submission that the risks of DMF should be better	

			managed by the restriction process.	
2241	2013/09/18 14:58	Air Liquide Deutschland GmbH, Company, Germany	Air Liquide Deutschland GmbH requests that "the use of DMF as a solvent and stabilizer for acetylene in bundles of gas cylinders, in multiple elements gas containers (MEGC) and in battery-vehicles" should be exempted from the authorisation process for the following reasons: 1. There is already existing EU legislation that adequately protects those exposed. 1.1. DMF contained in the acetylene distribution equipment is used in industrial settings where the risk is properly controlled by the implementation of the Community legislation on the protection of workers; namely the Chemical Agents Directive 98/24/EC (CAD). 1.2. That versus the risk causing DMF to be considered for SVHC there is directive 92/85/EEC on the protection of pregnant workers. For information all workers in EIGA retest facilities are male. 1.3. That there is established IOELV values, see directive 2009/161/EU. This defines an IOELV of 5ppm/15mg/m3. The workplace assessment of the exposure to DMF at EIGA members has shown that the exposure of workers is much lower than the IOELV. Furthermore due to the small amount of time in which acetylene gas cylinder are opened for the legally required 10 yearly retest, the average worker exposure is estimated to be less than 20 hours a year. 2. Any DMF contained as impurity in the acetylene flow coming out of the distribution equipment is burnt (destroyed) with the acetylene in the process of the final user of the acetylene. 3. That the use of DMF in bundles of cylinders, MEGC and battery-vehicles is safer than the only presently approved available alternate, acetone, because it eliminates the need to regularly and frequently disassemble the equipment for the make-up of the lost solvent required for safe transport of acetylene. This is a function of DMF's inherent physical property, much lower vapour pressure (described in the ECHA dossier on the properties of substance). Notes 1. Definitions and illustrations of "bundle of cylinders", MEGC and battery-vehicle is in the attachment. 2. The descriptions of the processes to retest cylinders and the survey of the exposure during these processes are in	Thank you for your comment. Please see response to comment 2456 (section I).

			the attachment (Section 4). On the strategy to manage the risks of DMF: Considering that the use in industrial settings is adequately protected by existing legislation and that the use by consumers is forbidden, Air Liquide Deutschland GmbH supports the comment made to the Annex XV dossier submission that the risks of DMF should be better managed by the restriction process.	
2240	2013/09/18 14:50	Air Liquide Deutschland GmbH, Company, Germany	Air Liquide Deutschland GmbH requests that "the use of DMF as a solvent and stabilizer for acetylene in bundles of gas cylinders, in multiple elements gas containers (MEGC) and in battery-vehicles" should be exempted from the authorisation process for the following reasons: 1. There is already existing EU legislation that adequately protects those exposed. 1.1. DMF contained in the acetylene distribution equipment is used in industrial settings where the risk is properly controlled by the implementation of the Community legislation on the protection of workers; namely the Chemical Agents Directive 98/24/EC (CAD). 1.2. That versus the risk causing DMF to be considered for SVHC there is directive 92/85/EEC on the protection of pregnant workers. For information all workers in EIGA retest facilities are male. 1.3. That there is established IOELV values, see directive 2009/161/EU. This defines an IOELV of 5ppm/15mg/m3. The workplace assessment of the exposure to DMF at EIGA members has shown that the exposure of workers is much lower than the IOELV. Furthermore due to the small amount of time in which acetylene gas cylinder are opened for the legally required 10 yearly retest, the average worker exposure is estimated to be less than 20 hours a year. 2. Any DMF contained as impurity in the acetylene flow coming out of the distribution equipment is burnt (destroyed) with the acetylene in the process of the final user of the acetylene. 3. That the use of DMF in bundles of cylinders, MEGC and battery-vehicles is safer than the only presently approved available alternate, acetone, because it eliminates the need to regularly and frequently disassemble the equipment for the make-up of the lost solvent required for safe transport of acetylene. This is a function of DMF's inherent physical	Thank you for your comment. Please see response to comment 2456 (section I).

			property, much lower vapour pressure (described in the ECHA dossier on the properties of substance). Notes 1. Definitions and illustrations of "bundle of cylinders", MEGC and battery-vehicle is in the attachment. 2. The descriptions of the processes to retest cylinders and the survey of the exposure during these processes are in the attachment (Section 4). On the strategy to manage the risks of DMF: Considering that the use in industrial settings is adequately protected by existing legislation and that the use by consumers is forbidden, Air Liquide Deutschland GmbH supports the comment made to the Annex XV dossier submission that the risks of DMF should be better managed by the restriction process.	
2237	2013/09/18 12:17	Industrievereinigung Chemiefaser e. V. , Industry or trade association, Germany		-
2236	2013/09/17 19:57	Pharmachemical Ireland, Industry or trade association, Ireland	The use of DMF in the manufacturing of pharmaceutical 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 is exempted from REACH authorisation requirements. This exemption would also include all PPORD uses of DMF (up to 50ts/pa) in the production of medicinal and veterinary products. Rationale for the Request for an Exemption as per Art 58(2) A directive is a legal instrument provided for in the EU Treaty and to date the majority of Community HSE legislation is based on the choice of the directive as the most appropriate legal instrument. It is binding in its entirety and obliges Member States to transpose it into national law within the deadlines clearly set out in the directive. A directive enters into force once it is published in the Official Journal of the EU. EU directives on safety and health at work have their legal foundation in Article 153 of the Treaty on the Functioning of the European Union (ex Article 137 TEC), which gives the EU the authority to adopt directives in this field. A wide variety of EU directives setting out minimum health and safety requirements for the protection of workers have since been adopted. Member States are free to adopt stricter (but not less strict) rules for the protection of workers when transposing EU directives into national law, and so legislative requirements in the field of	Thank you for your comment. Please see response to comment 2456 (section I).

			safety and health at work can vary across EU Member States. The decision to recommend DMF for inclusion in Annex XIV is based solely on occupational health risks (DMF is classified as toxic for reproduction category 1b). Those risks are already properly controlled (as outlined below) by the application of Directive 98/24/EC (Chemical Agents Directive), Directive 2009/161/EU (IOEL for DMF), Directive 92/85/EC (Pregnant Workers), Directive 2010/75/EU (Industrial Emissions Directive) and 2001/83/EC (Medicinal Products Directive) which impose minimum requirements that must be transposed into national legislation by EU Member States. 98/24/EC Chemical Agents Directive (CAD) Article 1 of Directive 98/24/EC This Directive ..... lays down minimum requirements for the protection of workers from risks to their safety and health arising, or likely to arise, from the effects of chemical agents that are present at the workplace or as a result of any work activity involving chemical agents. Article 6(2) of Directive 98/24/EC Substitution shall by preference be undertaken, whereby the employer shall avoid the use of a hazardous chemical agent by replacing it with a chemical agent or process which, under its condition of use, is not hazardous or less hazardous to workers' safety and health, as the case may be. Where the nature of the activity does not permit risk to be eliminated by substitution, having regard to the activity and risk assessment referred to in Article 4, the employer shall ensure that the risk is reduced to a minimum by application of protection and prevention measures, consistent with the assessment of the risk made pursuant to Article 4. These will include, in order of priority: • Design of appropriate work processes and engineering controls and use of adequate equipment and materials, so as to avoid or minimise the release of hazardous chemical agents which may present a risk to workers' safety and health at the place of work; • Application of collective protection measures at the source of the risk, such as adequate ventilation and appropriate organizational measures; Where exposure cannot be prevented by other means, application of individual protection measures including personal protective equipment. 1. We believe ECHAs previous interpretation of the minimum requirements as outlined in CAD is contrary to the principles of proportionality. The legal obligation on the	

			employer to put in place specific protection and prevention measures is in keeping with the principles of proportionality. A technical feasibility assessment of control measures beyond what is recommended by a chemical agents risk assessment is disproportionate. Note the clear intentions of CAD: "To ensure not only the protection of the health and safety of each individual worker but also to provide a level of minimum protection of all workers in the Community which avoids any possible distortion in the area of competition" (Preamble 4 of Directive 98/24/EC) 2009/161/EU Indicative OEL Values Directive Article 2 of Directive 2009/161/EU Member States shall establish national occupational exposure limit values for the chemical agents listed in the Annex, taking into account the Community values. 1. 98/24/EC (CAD) requires setting of indicative occupational exposure limit values (IOELVs) in all Member States (who are obligated to do transpose this and that their national limits must, at a minimum, be as stringent as the EU levels). DMF is referenced in Directive 2009/161/EU, establishing a third list of indicative occupational exposure limit values in implementation of Council Directive 98/24/EC and amending Commission Directive 2000/39/EC The following OEL has been set for DMF within EU law: 8 hour TWA: 5 ppm (15mg/m³), STEL (15 mins): 10 ppm (30mg/m³). Austria, Belgium, France, Germany, Ireland, Italy, Netherlands and UK are, to name but a few, Member States that have transposed this OEL into their National Legislation. PCI member companies have actual DMF monitoring data that can be shared with ECHA to show the controls used within our manufacturing facilities enables us to comply with the DMF OEL. 2. Furthermore, "A registrant is allowed to use an IOEL as a DNEL for the same exposure route and duration, unless new scientific information that he has obtained in fulfilling his obligations under REACH does not support the use of the IOEL for this purpose." . According to the ECHA guidance, IOEL values are valid DNELs to be accepted for occupational uses. If the CMR properties were considered when deriving the IOEL, there is no scientific reason for ECHA not to accept the IOEL unless new experimental data has been generated. In Summary DMF is referenced in 2009/161/EU and has been given a minimum OEL. Therefore 2009/161/EU should satisfy Art 58(2)	

			Existing Community Legislation. Not accepting this Directive as satisfying the requirements for an exemption under Article 58(2) undermines the legal authority of Directive 2009/161/EU and creates a situation of double regulation which is against the principle of the EU Commission's approach to "Smart Regulation". 92/85/EC Pregnant Workers, Recently Given Birth or Breast Feeding Article 5 • If the results of the assessment referred to in Article 4 (1) reveal a risk to the safety or health or an effect on the pregnancy or breastfeeding of a worker within the meaning of Article 2, the employer shall take the necessary measures to ensure that, by temporarily adjusting the working conditions and/or the working hours of the worker concerned, the exposure of that worker to such risks is avoided. • If the adjustment of her working conditions and/or working hours is not technically and/or objectively feasible, or cannot reasonably be required on duly substantiated grounds, the employer shall take the necessary measures to move the worker concerned to another job. • If moving her to another job is not technically and/or objectively feasible or cannot reasonably be required on duly substantiated grounds, the worker concerned shall be granted leave in accordance with national legislation and/or national practice for the whole of the period necessary to protect her safety or health. • The provisions of this Article shall apply mutatis mutandis to the case where a worker pursuing an activity which is forbidden pursuant to Article 6 becomes pregnant or starts breastfeeding and informs her employer thereof. 1. Directive 92/85 provides for the necessary measures to be taken by the employer in case of risk or effect on the pregnancy or breastfeeding of a worker In Summary Some active pharmaceutical ingredients by the very nature of their pharmacological action are Reprotoxins e.g. antimitotic drugs. Bulk API plants handling these substances (such as DMF) typically have reproductive hazard evaluation programmes in place covering APIs and solvents to protect the employee planning a pregnancy or recently become pregnant. Examples of risk reduction recommendations include additional PPE, delegating tasks to non-pregnant employees or banning such workers entering areas where DMF type substances are	

			handled. Therefore 92/85/EC should satisfy Art 58(2) Existing Community Legislation 2010/75/EU Industrial Emissions Directive IED Art 58: Substitution of Hazardous Substances Substances or mixtures which, because of their content of volatile organic compounds classified as carcinogens, mutagens, or toxic to reproduction under Regulation (EC) No 1272/2008, are assigned or need to carry the hazard statements H340, H350, H350i, H360D or H360F, shall be replaced, as far as possible by less harmful substances or mixtures within the shortest possible time IED Art 59(5) Control of Emissions: The emissions of either volatile organic compounds which are assigned or need to carry the hazard statements H340, H350, H350i, H360D or H360F or halogenated volatile organic compounds which are assigned or need to carry the hazard statementsH341 or H351, 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 set out in Part 4 of Annex VII . 1. DMF is used in Bulk Pharma manufacturing facilities to manufacture API; all Bulk Pharma API manufacturing facilities are required to have a PPC Permit (soon to be Industrial Emissions Permit under the Industrial Emissions Directive). This requirement is referenced in Annex I of the IED (section 4.5). 2. The IED (and the previous directives that have now been included within it including 2000/76/EC) requires permit holders who use H360D compounds to replace them, as far as possible, by less harmful substances within the shortest period of time. DMF is a H360D substance 3. The IED requires permit holders that emissions of H360D substances shall be controlled under contained conditions as far as technically and economically feasible to safeguard public health and the environment. DMF is a H360D substance. 4. DMF used in the API manufacturing stage is collected after use and (in the majority of cases) is incinerated (under the Waste Incineration Directive 2000/76/EC soon to be incorporated into the Industrial Emissions Directive). Where DMF is not incinerated, it is recycled. In Summary All bulk API facilities using DMF must have an Industrial Permit to operate. That permit lays down minimum conditions to	

			protect the environment as well as requiring substitution of H360D substances. The EU Commission does not need to implement further legislation to require the substitution of H360D substances (that are used in an IED permitted facility). All waste DMF is handled appropriately. Community Legislation (2010/75/EU) properly controls the emissions of DMF associated with the manufacture of APIs and the use of the API during drug manufacture. Therefore 2010/75/EU should satisfy Art 58(2) Existing Community Legislation. 2010/75/EU Industrial Emissions Directive (Solvents) IED Annex VII Technical Provisions relating to Installations and Activities using Organic Solvents Part 1(Activities): (8). Manufacturing of pharmaceutical products: The chemical synthesis, fermentation, extraction, formulation and finishing of pharmaceutical products and, where carried out at the same site, the manufacture of intermediate products IED Annex VII Technical Provisions relating to Installations and Activities using Organic Solvents Part 2(Thresholds and Emission Limit Values): (20). Manufacturing of pharmaceutical products: >50ts/yr. of solvents; waste gases emission limit 20mg/m³; total ELV is 15% of solvent output IED Art 59(1) Control of Emissions: Member States shall take the necessary measures to ensure that each installation complies with either of the following: (a) the emission of volatile organic compounds from installations shall not exceed the emission limit values in waste gases and the fugitive emission limit values, or the total emission limit values, and other requirements laid down in Parts 2 and 3 of Annex VII are complied with Existing Community Legislation (2010/75/EU) properly controls the emissions of DMF associated with the manufacture of APIs and the permitting/use/storage of the solvent during drug manufacture. One objective of the IED is to prevent or reduce the direct and indirect effects of emissions of VOCs during the manufacture of pharmaceutical products into the environment, mainly into air, and the potential risks to human health, by providing measures and procedures to be implemented for certain activities. The IED already governs and manage the risks that the inclusion of Pharma uses of DMF in REACH Annex XIV seeks to manage. Article 62 (5b) of the REACH Regulation would suggest that this is also the case. In Summary All bulk API facilities using >50ts/yr. of solvents (including DMF)	

			must have an Industrial Permit to operate. That permit lays down maximum emission to air limits for solvents, therefore the IED provides minimum emission to air standards in API Bulk Manufacturing facilities using >50ts/yr. of solvents. This shows that DMF is properly controlled. Therefore 2010/75/EU should satisfy Art 58(2) Existing Community Legislation. Medicinal Products Directive: Directive 2001/83/EC & Regulation (EC) No 726/2004 1. The EU medicinal regulatory system protects public health and secures the availability of medicinal products for EU citizens by requiring all such products to have been granted a Marketing Authorisation (MA) of before they are placed on the EU market. These MAs are granted only if the manufacturing process complies with the EU quality standards known as "good manufacturing practices." After a MA is issued, MA holders may not introduce any changes into the manufacturing process without the consent of the Member State competent authority. Finally, once a medicinal product has been authorised and placed on the EU market, its safety is monitored throughout its entire lifespan to ensure that, in case of adverse reactions that present an unacceptable level of risk under normal conditions of use, it is rapidly withdrawn from the market. This is done through the EU system of "Pharmacovigilance" set out in the Medicinal Products Directive (MPD). 2. We believe that the MPD does properly control the risks of the use of DMF within the manufacture of an API that 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 MA of a medicinal product referred to in Article 40 of Directive 2001/83/EC is obliged "to comply with the principles and guidelines of good manufacturing practice (GMP)" as laid down by community law. Principles and guidelines of GMP require impurity testing of pharmaceutical ingredients to ensure that specific threshold limits for residual solvents are met. All Pharmaceutical products that are impacted by such solvents have the information included in the MA which can be withdrawn if the pharmaceutical product does not meet the residual solvent specification. This concentration limit is enforced via the Member State relevant Health Regulator (e.g. MHRA in the UK). EMA guidance on residual solvents (EMA/CHMP/ICH/82260/2006) contains specific limits for DMF (PDE 8.8mg/day and 880ppm). 3. Since the residual amount of DMF in the eventual pharmaceutical product is safety-limited by the EMA (Guideline	

			for Residual Solvents in practice virtually all the DMF used during manufacture of the API would be present in the waste streams that are then disposed of via incineration as hazardous waste (under the Waste Incineration Directive 2000/76/EC soon to be incorporated into the Industrial Emissions Directive). Where DMF is not incinerated, it would be purified and recycled into DMF that can be used again. 4. Recital 111 of REACH cautions against mixing the policy aims of REACH with the policy aims of the European Medicines Agency (EMA). The legislative history of REACH reflects the special relationship between the chemical and medicinal regulatory regimes. The Commission expressly addressed the interaction between the two regimes when it proposed REACH, indicating how it would avoid potential overlaps (thereby showing that the Commission was (i) aware of the potential overlap between REACH and the medicines legislation and (ii) it aimed to avoid such overlap): "Certain uses of substances are not subject to authorisation because their human health and environmental effects are considered to be addressed by equivalent Community legislation. It would be unreasonable to subject such uses to two systems with the cost and resources this would imply. The Commission will propose a modification of the legislation on medicinal products for human use and veterinary use respectively to address risks related to the environment. This will be part of the benefit/risk assessment which has to be positive as a prerequisite for approval of the medicinal product". [Emphasis added] In Summary First, the REACH Regulation was not meant to overlap with or impede the functioning of this Medicinal regulatory regime. Indeed, substances used in medicinal products for human and veterinary use and falling under the scope of the Medicinal Products Legislation are specifically exempted from the REACH authorisation requirements. Secondly, in line with the text of REACH, the history of the Regulation, and the proportionality principle, we believe that ECHA should avoid any conflict with the EMA's specific authority to approve the market placement of medicinal products. Thirdly, 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). Therefore 2001/83/EC and its associated Guidance should also help satisfy our compliance with the conditions for exemption set down in Art 58(2) with regard to existing Community Legislation. Conclusions • In the comments above, we have cited various EU laws which, collectively and individually, meet the conditions imposed for the exemption under Article 58.2 of REACH • 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, not only by REACH 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… • Pharmaceutical manufacturing uses of DMF meet the requirements set out in Article 58 (2) of REACH and on this basis should be exempted from REACH Authorisation requirements; • Our uses of DMF as an aprotic solvent are already governed by existing EU legislation setting minimum requirements for the proper control of risks to human health or the environment; • There will be no direct or net environmental benefit by including Pharma uses of DMF in Annex XIV; • Use of DMF in pharmaceutical manufacturing is not widely dispersive, and the scoring system applied in Annex XV would not qualify DMF as used in Pharma for prioritization • REACH article 62(5)(b)(i) suggests that an Annex XIV listed substance handled in a facility that is permitted by Directive 96/61/EC (soon to be incorporated into 2010/75/EU IED) doesn't need to consider risks from Human Health or the Environment when submitting an application for an Authorised Use of that Substance. This therefore exempts annex XIV listed substances from Authorisation if the substance is used in an IPPC Permitted facility and no economic or technically feasible substitution substances exist.	
2234	2013/09/17	Fedustria, Industry or trade	Use exempted from the authorisation requirement	Thank you for your comment.

	16:11	association, Belgium	Opposite to the conclusion in the draft background document for DMF, we are of the opinion that specific Community legislation is in force that would allow exemption of use from the authorisation requirement on the basis of Article 58(2) of the REACH Regulation. Risks properly controlled by existing EU legislation There is sufficient community legislation in place imposing the substitution principle and risk management measures relating to the protection of the workers and environment. Protection of the health and safety of workers DMF was included in the third list of indicative occupational exposure limit values (IOELVs) set up by Commission Directive 2009/161/EU (17.12.2009). IOELVs are health-based values derived from the most recent scientific data and correspond to threshold levels of exposure below which no detrimental effects are expected after short-term or daily exposure to the substance over a working life time. Member States were subsequently required to establish a national occupational exposure limit value, taking into account the Community limit value of DMF by 18 December 2011. Therefore, Directive 2009/161/EU properly addresses the occupational use of DMF and health risk in connection with its use. Environmental protection We are convinced that Directive 1999/13/EC on the limitation of emissions of volatile organic compounds due to the use of organic solvents in certain activities and installations establishes (VOC directive) the correct framework to guarantee that emissions form processes using DMF in the categories of activity described in Annex 1 (of Directive 1999/13/EC) are well controlled. The coating processes in the textile sector using DMF are explicitly mentioned in this annex. The VOC directive does not only set a strict emission limit value of 2 mg/Nm3 for VOC-discharges containing substances that carry the risk phrase R61 (as DMF does), it also obliges that substances or preparations containing VOCs with the risk phrases R61 shall be replaced as far as possible by less harmful substances or preparations within the shortest possible time (see article 5 point 6 of the VOC directive). The activities described in annex 1 of Directive 1999/13/EC are operated under conditions guaranteeing controlled exposure (public health and the environment). Monitoring and reporting obligations for companies as well as for member states are part of the directive. In other words as the VOC-Directive has the same objective as	Please see response to comment 2456 (section I).

			what is intended by authorisation (replacing by less harmful substances) under REACH, there is no need at all to apply additional obligations to DMF. This very same obligation exist already for years under EU-legislation. The requirement to apply for an authorisation will hence not improve the protection of the environment or the workers. As authorisation is not only a burdensome procedure but also very costly for the textile coating industry that consists mainly of SME, this will result in an additional impediment of the competitiveness with regard to the non-European enterprises. Therefor we are of the opinion that textile coating as described in annex I of the directive 1999/13/EC (i.e. "any activity in which a single or multiple application of a continuous film of a coating is applied to textile and fabric …") should be exempted from authorisation.	
2233			Air Products comments on the use of DMF in acetylene cylinders placed within bundles/packs. Air Products notes that the reason DMF is of concern is that it has been shown in laboratory studies on rats, rabbits etc. to cause deformity amongst new borne, though as yet there is no study implying harm to humans. That testing has showed that the hazard was continuous long term (multi year) exposure of pregnant animals to high doses (40 to 100 times the 8 hour occupational exposure limits). In Air Products the exposure of workers to DMF is restricted to males, with limited duration (approximately 20 hours per year) and to levels which available industrial analysis cannot measure i.e. less than 0.1ppm. To Air Products it seems excessive to use legislation that will effectively lead to the long term banning of DMF from all European industries when it is only a limited subset of sectors and uses that expose females to DMF for long periods at concentrations near or above the occupational exposure limits. Europe will put itself at economic disadvantage if it follows this path. Europe has more suitable legislation already available (safeguard of worker which can stop employers allowing females to be exposed to DMF & restriction of use which can stop processes involving high concentrations of DMF exposure) with which to protect those exposed to the hazards of DMF.	Thank you for your comment. Please refer to response to comments 2488, 2456 and 2427 in section I.
2232	2013/09/17 14:14	Company, Denmark	DMF is already regulated by a lot of different EU directives. DMF is included in the third list of indicative occupational exposure limit values (IOELVs) set up by Commission Directive 2009/161/EU (17.12.2009). IOELVs are health-based values derived from the most recent scientific data and correspond to threshold levels of exposure below which no detrimental effects	Thank you for your comment. Please see response to comment 2456 (section I).

			are expected after short-term or daily exposure to the substance over a working life time. Member States were subsequently required to establish a national occupational exposure limit value, taking into account the Community limit value of DMF by 18 December 2011. Therefore, Directive 2009/161/EU properly addresses the occupational use of DMF and health risk in connection with its use at industrial sites. Since the vapour pressure of DMF at 20°C is 0.38 kPa which is above 0.01 kPa DMF is considered a volatile organic compound (VOC) according to EU's VOC Solvents Emissions Directive (1999/13/EC). This directive provides a very effective regulatory policy instrument for the reduction of industrial emissions of volatile organic compounds (VOCs). It requires installations to comply either with the emission limit values set out in the Directive or with the requirements of the so-called reduction scheme. As a result of the classification of DMF as toxic to reproduction additional existing EU legislation provide further measures to ensure safe use of the substance. These include Council Directive 98/24/EC (Protection of health and safety of workers from risks related to chemical agents at work) and Council Directive 92/85/EEC (Measures to encourage improvements in the safety and health at work of pregnant workers and workers who have recently given birth or are breastfeeding). Conclusion Since the industrial use of DMF is already regulated in all these ways we recommend that if the substance should be included in Annex XIV the industrial use should be exempted from authorisation.	
2231	2013/09/17 11:34	Panasonic Industrial Devices Materials Europe GmbH, Company, Austria	At the location Enns (Austria), PIDMEU is producing base materials for printed circuit boards. The products are made by combining Prepregs (glass cloth coated with Epoxy resin) and Copperfoil. In order to produce Prepregs, a varnish, consisting mainly of epoxy resin, hardener and catalyst dissolved in organic solvents, is prepared. DMF currently is the technically preferred solvent for special hardener- in respect of safety, health and economical issues there are no alternatives leading to the same result. DMF is delivered in tank lorries and stored in a closed tank. It is transported through pipes to the mixing room into tanks where the varnish is blended. The prepared varnish is transported to the impregnation area through pipes. Glass cloth from large rolls is impregnated with the varnish by housed-in dipping pan. The solvent in the	Thank you for your comment. Please refer to response to your comment in section I.

			varnish is vaporized in a closed drying chamber. Afterwards it is burnt in a thermal incinerator whose emissions are kept to a minimum. Moreover checks are conducted regularly in order to keep emissions below authority Iimits. The final product is mainly used for our CCL production. Additionally the product is sold to producers of printed circuits but in no case to end users. Safety measures Technical measures Local authority permits a MAK value Iimit of 4 mg/m3 in this area. This Iimit is checked regularly. Nitrogen is used to hinder further emissions during the mixing procedure. The treating area is Iabelled as Ex-Zone and the exposure regarding solvents is checked regularly. Organisational measures Due to special protection gear the staff is not exposed directly to DMF. Special internal safety instructions as well as regular safety training are provided. Consequences for DMF restrictions for PIDMEU We employ 130 people at our plant in Austria. In the case of DMF being severely restricted we see no other possibility but to shut down our production.	
2225	2013/09/16 19:33	Company, France	N,N-dimethylformamide (DMF) is a frequently used important solvent for the production of chemical intermediates used for the production of APIs. No suitable alternative solvents exist that do not show similar hazardous properties or are technically equivalent. For this use, DMF is handled by professional trained workers and risk management measures are in place to minimize exposition. That's why we ask to exempt this specific use from authorisation.	Thank you for your comment. Please see response to comment 2456 (section I).
2220	2013/09/16 12:27	Company Finland	Usage as solvent in manufacturing active pharmaceutical ingredients (API). 1) Its usage today already is under REACH legislation as strictly controlled conditions. 2) DMF is highly difficult to change to another solvent because of its good solubility properties. 3) DMF is so-called CMR substance and there for PCAS Finland has tried to change it to another solvent, but we have not succeeded to do that.	Thank you for your comment. Please see response to comment 2456 (section I).

			4) The processes of API´s are registered to authorities before those will get the sales licenses. After that process it is very difficult to make changes for example change of solvent. 5) The use of authorised substance is very expansive and high-risk, because authority can at any time decide to stop of usage of the authorisate substance. 6) DMF is commonly used solvent in API´s manufacturing processes and its restriction of usage will reduce European API manufactures competitivity in the future.	
2214	2013/09/13 16:25	Company United Kingdom	We would propose that all current industrial uses which are subject to COSHH and EA regulation are exempted from any Authorisation process. This would include synthesis and coating, using the solvent as a carrier this would be justified because they are adequately controlled already by other legislation.	Thank you for your comment. Please see response to comment 2456 (section I).
2206	2013/09/11 08:26	Company Slovenia	DMF use in pharmaceutical use should be exempted from the authorisation because there is very low exposure to consumers and the environment because of best available techology is used for handling this substance. Industrial and professional personnel which are well trained, using the substance for pharmaceutical and analytical purposes. The disposal of the substance is also well controlled.	Thank you for your comment. Please see response to comment 2456 (section I).
2199	2013/09/10 12:50	Company United Kingdom	PROC 5 We are subject to a Local Authority Pollution Prevention Control (LAPPC) Operating Permit involving VOC emission abatement in accordance with the requirements of the primary legislation, the Solvents Directive 1999/13/EC.	Thank you for your comment. Please see response to comment 2456 (section I).
2198	2013/09/09 15:32	International organisation United Kingdom	PROC 0: other - solvent : exemption under article 58.2 for the use of DMF as an industrial process solvent.	Thank you for your comment. Please see response to comment 2456 (section I).
2194	2013/09/05 17:10	Company Netherlands	The use of DMF as a solvent for polymers. The use of DMF as a solvent is completely safe.	Thank you for your comment. Please see response to comment 2456 (section I).
2193	2013/09/05 14:44	PENNEL & FLIPO Industry or trade association Belgium	Dissolution de TPU; le solvant est brulé dans un incinérateur-L produit fini ne contient pas de DMF	Thank you for your comment. Please see response to comment 2456 (section I).
2191	2013/09/04 17:18	Cymaco Nederland BV Company Belgium	DMF is widely used as solvent to stabilise acetylene in gas cylinders & bundles. At the time of the mandatory periodical inspection of the cylinders and bundles, the DMF contents is measured and, if needed, adjusted to its initial value determined by the gas cylinder manufacturer (EN 12755). In	Thank you for your comment. Please see response to comment 2456 (section I).

		Netherlands	the retest & inspection facility, the DMF addition is executed in a closed system, the area is well-ventilated and the operator protected with a full-facemask with supplied air system, chemical resistant gloves and suitable clothing. Risks on accidental emissions have been reduced. The yearly quantity used for solvent adjusting is less than 0.5 tons.	
2179	2013/09/02 10:04	Polski Koncern Naftowy ORLEN S.A. Company Poland	Use as solvent (e.g. in purification, crystallisation, extraction operations or as reagent, catalyst or cross-linking agent) in synthesis of chemicals. Our company is a downstream user of N,N-Dimethylformamide (DMF). DMF is used as selective diluent in low volume (approx. 20 t/month) in extractive distillation during production of buta-1,3-diene (the basic raw material for production of butadiene-styrene rubbers). The substance is used in closed process with occasional controlled exposure (e.g. sampling, maintenance). 1-on-1 alternatives are not readily available for this application, because our Butadien Separation Plant is designed only with the participation of DMF.	Thank you for your comment. Please see response to comment 2456 (section I).
2170	2013/08/28 12:56	Company United Kingdom	No comments.	-
2165	2013/08/27 18:39	Company United Kingdom	COMMISSION DIRECTIVE 2009/161/EU of 17 December 2009 if the indicative were to be mandatory	Thank you for your comment. Please refer to response to your comment in section I.
2161	2013/08/21 17:02	AGTC Bioproducts Ltd Company United Kingdom	DIMETHYLFORMAMIDE CAS 68-12-2 EC 200-679-5, SVHC list This material is used extensively in the synthesis of peptides for use in basic research. It is invariably handled in a controlled environment (synthetic laboratories are very used to handling dangerous materials) and as far as we can see represents a very low hazard to the people working directly with the material. The synthesis is carried out in a sealed environemt, the waste is collected and stored in sealed containers and disposed of in the authorised and approved manor as required by the institute in which the laboratory is located. In our view this material does not present a significant risk to the operatives and the and the end products of their work contribute significantly to the overall well being of the human race.	Thank you for your comment. Please refer to response to your comment in section I.
2152	2013/08/19 09:59	European Industrial Gases Association (EIGA) Industry or trade association	EIGA requests that "the use of DMF as a solvent and stabilizer for acetylene in bundles of gas cylinders, in multiple elements gas containers (MEGC) and in battery-vehicles" should be exempted from the authorisation process for the following	Thank you for your comment. Please see response to comments 2456 and 2427 in section I.

		Belgium	reasons: 1. There is already existing EU legislation that adequately protects those exposed. 1.1. DMF contained in the acetylene distribution equipment is used in industrial settings where the risk is properly controlled by the implementation of the Community legislation on the protection of workers; namely the Chemical Agents Directive 98/24/EC (CAD). 1.2. That versus the risk causing DMF to be considered for SVHC there is directive 92/85/EEC on the protection of pregnant workers. For information all workers in EIGA retest facilities are male. 1.3. That there is established IOELV values, see directive 2009/161/EU. This defines an IOELV of 5ppm/15mg/m3. The workplace assessment of the exposure to DMF at EIGA members has shown that the exposure of workers is much lower than the IOELV. Furthermore due to the small amount of time in which acetylene gas cylinder are opened for the legally required 10 yearly retest, the average worker exposure is estimated to be less than 20 hours a year. 2. Any DMF contained as impurity in the acetylene flow coming out of the distribution equipment is burnt (destroyed) with the acetylene in the process of the final user of the acetylene. 3. That the use of DMF in bundles of cylinders, MEGC and battery-vehicles is safer than the only presently approved available alternate, acetone, because it eliminates the need to regularly and frequently disassemble the equipment for the make-up of the lost solvent required for safe transport of acetylene. This is a function of DMF's inherent physical property, much lower vapour pressure (described in the ECHA dossier on the properties of substance). Notes 1. Definitions and illustrations of "bundle of cylinders", MEGC and battery-vehicle is in the attachment. 2. The descriptions of the processes to retest cylinders and the survey of the exposure during these processes are in the attachment (Section 4). On the strategy to manage the risks of DMF: Considering that the use in industrial settings is adequately protected by existing legislation and that the use by consumers is forbidden, EIGA supports the comment made to the Annex	

			XV dossier submission that the risks of DMF should be better managed by the restriction process.	
2108	2013/07/24 17:57	Company France	N,N-Dimethylformamide – Comments on uses that should be exempted (2013.07.10) N,N-Dimethylformamide could be used as an intermediate under strictly controlled conditions and is, in this case, excluded from authorisation process accordingly to article 2.8.b of REACH regulation. One of these uses in synthesis is the so-called "Vilsmeier-Haack" reaction in which N,N-Dimethylformamide is also used as the synthesis solvent, as it is generally not possible to use a co-solvent which one would also reacts on "Vilsmeier-Haack" reactant. Considering that: -N,N-Dimethylformamide is loaded in the reaction vessel, respecting strictly controlled conditions. -No N,N-Dimethylformamide could be detected in synthesised substance, as unreacted N,N-Dimethylformamide (solvent) is eliminated in waste water and that these waste water is necessarily burned being not biodegradable. We estimate that the use of N,N-Dimethylformamide as solvent in reaction in which N,N-Dimethylformamide is also a reactant should be exempted from authorisation if strictly controlled conditions are met. Contact Person: Jean-Pierre GUILLOT, REACH Coordinator INTEROR S.A. Z.I. des Dunes Rue des Garennes F-62100 CALAIS France Tel: +33 (0)321.97.06.21 jean-pierre.guillot@interor.com	Thank you for your comment. Please see response to comments 2456 (section I).
2099	2013/06/25 10:35	Individual France	DMF is used in the synthesis of an Active Pharmaceutical Ingredient : oxybutine chlorhydrate. Because of the Pharmaceutical agreement, it is not possible to substitute this raw material. If this substance is on the authorisation list it will be difficult for the API manufacturer to buy it and also to manufacture the API.	Thank you for your comment. Please see response to comment 2456 in section I (sub-heading 'other reason to justify exemption').

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

#	Date	Submitted by (name, Organisation/MSCA)	Comment	Response
2473	2013/09/23 19:31	ChemSec, International NGO, Sweden	ChemSec supports the proposal of ECHA to not allow any review periods.	Thank you for your comment. Please note that all authorisation decisions will include specific review periods. ECHA's opinion is that these should be decided on a case by case basis and not upfront, i.e. in the Annex XIV entries. See also response to comment 2455 in this section.
2455	2013/09/23 17:38	European Diagnostic Manufacturers Association (EDMA), Industry or trade association, Belgium	EDMA does not support Authorisation as the most appropriate risk management option for the reasons mentioned under the 'General Comments' section. If the EU should regardless decide to proceed with including DMF on REACH Annex XIV, the IVD sector would require review periods of 7-10 years in length considering the hundreds of products which would be impacted, the majority SME nature of our sector, and the extensive re-validation and re-registration required both in the EU and internationally.	Thank you for your comment and the information provided regarding your sector of use. 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. ECHA opinion is that 'upfront' specified review period for the use of DMF is not warranted in the recommendation for Annex XIV inclusion. Note that setting 'upfront' review periods 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. 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 RAC's and SEAC's approach for establishing the length of the review period.(http://echa.europa.eu/documents/10162/13580/seac_rac_review_period_authorisation_en.pdf) Please also refer to response to your comments in the other sections.
2449	2013/09/23 17:05	Company, Germany	as mentioned above 7 to 10 years	Thank you for your comment. Please refer to response to comment 2455 in this section.
2434	2013/09/23 15:51	EFPIA, Industry or trade association, Belgium	No Comment	-
2431	2013/09/23 15:37	GIFAS, Industry or trade association, France	Please refer to attached document	Thank you for your comment. Please refer to response to your comments in the other sections. Also consider response to comment 2455 in this section.
2423	2013/09/23 15:01	Company, Czech Republic	Above mentioned.	Please refer to response to your comments in the other sections. Also consider response to comment 2455 in this section.
2356	2013/09/20 20:21	Company, France	No comment	-
2347	2013/09/20 18:27	Company, Ireland	N/A	-
2343	2013/09/20 17:33	Individual, Italy	According to Article 58(2) are to be considered the exemptions for categories of uses listed above because there is already existing Community legislation that imposes minimum	Thank you for your comment. Please refer to response to your

			requirements to control the risks connected to the use of DMF. About reprotoxic substances like DMF, specific measures to ensure safe use are already provided in Council Directive 98/24/EC (Protection of health and safety of workers from risks related to chemical agents at work) and Council Directive 92/85/EEC (Measures to encourage improvements in the safety and health at work of pregnant workers and workers who recently given birth or are breastfeeding). Furthermore, there is a restriction in REACH (annex XVII, entry 30) for substances classified as reprotoxic cat. 1 and cat.2. Also, VOC-Directive 1999/13/EC gives requirements already met by industries in work processes, so Authorization dossier will not add other added values to prevent risks to human health and environment. DMF is included in the third list of indicative occupational exposure limit values (IOEL) established by Commission Directive 2009/161/EU of 17 December 2009 (TLV-TWA: 15 mg/m3, 5 ppm; TLV-STEL: 30 mg/m3; 10 ppm). According to the ECHA guidance, IOEL values are valid DNELs to be accepted for occupational uses. If the CMR properties were considered when deriving the IOEL there is no scientific reason for ECHA not to accept the IOEL unless new experimentally data has been generated. The fact that a substance is an SVHC candidate or recommended for authorization is not new scientific information with respect to health effect. In addition, the prevention measures taken during DMF processing include periodical and continual monitoring on workers through: - analysis of the concentrations of a chemical marker in a human biological media - Biological Exposure Index (BEI); - analysis of a substance's concentration in the ambient air in the workplace (indoor air quality); - inhalation exposure of workers (TLV-TWA and TLV-STEL values). All the values obtained where always below the limits indicated by Community legislation. In conclusion, DMF is not intended for consumer or professional use but only for industrial use. All the industrial uses described above, properly control the risks connected to human health and the environment.	comment in section I.
2312	2013/09/20 12:57	CHINOIN Private Co. Ltd., Company, Hungary	No Comment	-

2298	2013/09/20 11:06	Assogastecnici/Federchimica, Industry or trade association, Italy	With respect to the review periods, Assogastecnici asks to take into account the following considerations that EIGA, the European Industrial Gases Association, already submitted in its own comments to this public Consultation: 1) Lack of available alternative DMF has certain physical properties which make it necessary for a proportion of the users of acetylene (principally its low vapour pressure which leads to low carryover into the acetylene gas). Historically this was not so important but some industries where the technology has improved require this higher grade and without it they will have to close. If the European Union stops the use of DMF in acetylene service then these industries will have to find an alternative. At the moment there is no alternative solvent, acetone is not sufficient, so until an alternative can be developed those industries would have to relocate outside the European Union. 2) Time taken to develop an alternative DMF is relatively new to the acetylene business, but even so it has been known of for more than thirty years. If an alternative was found tomorrow it will take more 10 years to undertake the necessary testing (to achieve approval under European Standard EN1800: Transportable gas cylinders - Acetylene cylinders - Basic requirements, definitions and type testing) followed by the practical evaluation by the end users. The finding of an effective alternative that has lesser risks than DMF is likely to present a major challenge for the industry with a low probability of success. 3) Long life of the equipment being impacted Cylinders in acetylene service have a typical lifetime of 50 or more years, cylinders that are 60,70 or more years old are not unknown. All DMF cylinders in acetylene service are at most fifteen years old. The typical sunset date of 18mths after the addition of the substance to annex XIV is not appropriate to this equipment. If applied then this equipment will have to be scrapped prematurely. The total population of acetylene cylinders in DMF service in Europe is estimated at more than 150 000. 4) Time taken to replace DMF equipment There is limited production capacity for new acetylene cylinders both in the European Union and World Wide (<3% of the total of equipment in service per year). If those cylinders in DMF service had to be replaced tomorrow then the manufacture of the new equipment will take in excess of five years, assuming no other equipment was manufactured. As noted above there	Thank you for your comment. Please refer to response to comment 2455 in this section. Also consider response to your comments in the other sections.

			is no off the shelf replacement solvent. 5) Limited amount of DMF The use of DMF as a solvent for acetylene cylinders is very small, less than 0.1% of the total DMF used in Europe. The application of review periods based upon major users where the turnover of DMF is quick to a sector where the amount of DMF is minor and the turnover is very slow is inappropriate.	
2286	2013/09/19 20:35	Company, Ireland	n/a	-
2285	2013/09/19 19:45	Individual, France	Diagnostica Stago wishes to comment on public consultation relating to a product made with DMF. See attachment confidential document.	Thank you for your comment. Please refer to response to your comments in the other sections.
2284	2013/09/19 19:31	Individual, France	Diagnostica Stago wishes to comment on public consultation relating to DMF. See attached confidential document.	Thank you for your comment. Please refer to response to your comments in the other sections.
2246	2013/09/18 16:38	The Linde Group, Region Central and Northern Europe, Company, Germany	EIGA makes the following comments regarding the review periods 1) Lack of available alternative DMF has certain physical properties which make it necessary for a proportion of the users of acetylene (principally its low vapour pressure which leads to low carryover into the acetylene gas). Historically this was not so important but some industries where the technology has improved require this higher grade and without it they will have to close. If the European Union stops the use of DMF in acetylene service then these industries will have to find an alternative. At the moment there is no alternative solvent, acetone is not sufficient, so until an alternative can be developed those industries would have to relocate outside the European Union. 2) Time taken to develop an alternative DMF is relatively new to the acetylene business, but even so it has been known of for more than thirty years. If an alternative was found tomorrow it will take more 10 years to undertake the necessary testing (to achieve approval under European Standard EN1800: Transportable gas cylinders - Acetylene cylinders - Basic requirements, definitions and type testing) followed by the practical evaluation by the end users. The finding of an effective alternative that has lesser risks than DMF is likely to present a major challenge for the industry with a low probability of success. 3) Long life of the equipment being impacted	Thank you for your comment. Please refer to response to comment 2455 in this section and to response to your comments in the other sections.

			Cylinders in acetylene service have a typical lifetime of 50 or more years, cylinders that are 60,70 or more years old are not unknown. All DMF cylinders in acetylene service are at most fifteen years old. The typical sunset date of 18mths after the addition of the substance to annex XIV is not appropriate to this equipment. If applied then this equipment will have to be scrapped prematurely. The total population of acetylene cylinders in DMF service in Europe is estimated at more than 150 000. 4) Time taken to replace DMF equipment There is limited production capacity for new acetylene cylinders both in the European Union and World Wide (<3% of the total of equipment in service per year). If those cylinders in DMF service had to be replaced tomorrow then the manufacture of the new equipment will take in excess of five years, assuming no other equipment was manufactured. As noted above there is no off the shelf replacement solvent. 5) Limited amount of DMF The use of DMF as a solvent for acetylene cylinders is very small, less than 0.1% of the total DMF used in Europe. The application of review periods based upon major users where the turnover of DMF is quick to a sector where the amount of DMF is minor and the turnover is very slow is inappropriate. On the strategy to manage the risks of DMF: Again EIGA, on the basis of its arguments with the review periods, would support the comment made to the Annex XV dossier submission that the risks of DMF should be better managed by the restriction process.	
2241	2013/09/18 14:58	Air Liquide Deutschland GmbH, Company, Germany	Air Liquide Deutschland GmbH makes the following comments regarding the review periods 1) Lack of available alternative DMF has certain physical properties which make it necessary for a proportion of the users of acetylene (principally its low vapour pressure which leads to low carryover into the acetylene gas). Historically this was not so important but some industries where the technology has improved require this higher grade and without it they will have to close. If the European Union stops the use of DMF in acetylene service then these industries will have to find an alternative. At the moment there is no alternative solvent, acetone is not sufficient, so until an alternative can be developed those industries would have to relocate outside the European Union. 2) Time taken to develop an alternative	Thank you for your comment. Please refer to response to comment 2455 in this section and to response to your comments in the other sections.

			DMF is relatively new to the acetylene business, but even so it has been known of for more than thirty years. If an alternative was found tomorrow it will take more 10 years to undertake the necessary testing (to achieve approval under European Standard EN1800: Transportable gas cylinders - Acetylene cylinders - Basic requirements, definitions and type testing) followed by the practical evaluation by the end users. The finding of an effective alternative that has lesser risks than DMF is likely to present a major challenge for the industry with a low probability of success. 3) Long life of the equipment being impacted Cylinders in acetylene service have a typical lifetime of 50 or more years, cylinders that are 60,70 or more years old are not unknown. All DMF cylinders in acetylene service are at most fifteen years old. The typical sunset date of 18mths after the addition of the substance to annex XIV is not appropriate to this equipment. If applied then this equipment will have to be scrapped prematurely. The total population of acetylene cylinders in DMF service in Europe is estimated at more than 150 000. 4) Time taken to replace DMF equipment There is limited production capacity for new acetylene cylinders both in the European Union and World Wide (<3% of the total of equipment in service per year). If those cylinders in DMF service had to be replaced tomorrow then the manufacture of the new equipment will take in excess of five years, assuming no other equipment was manufactured. As noted above there is no off the shelf replacement solvent. 5) Limited amount of DMF The use of DMF as a solvent for acetylene cylinders is very small, less than 0.1% of the total DMF used in Europe. The application of review periods based upon major users where the turnover of DMF is quick to a sector where the amount of DMF is minor and the turnover is very slow is inappropriate. On the strategy to manage the risks of DMF: Again Air Liquide Deutschland GmbH, on the basis of its arguments with the review periods, would support the comment made to the Annex XV dossier submission that the risks of DMF should be better managed by the restriction process	
2240	2013/09/18 14:50	Air Liquide Deutschland GmbH, Company, Germany	Air Liquide Deutschland GmbH makes the following comments regarding the review periods 1) Lack of available alternative DMF has certain physical properties which make it necessary for a proportion of the users of acetylene (principally its low vapour	Thank you for your comment. Please refer to response to comment 2455 in this section and to response to your comments in the other sections.

			pressure which leads to low carryover into the acetylene gas). Historically this was not so important but some industries where the technology has improved require this higher grade and without it they will have to close. If the European Union stops the use of DMF in acetylene service then these industries will have to find an alternative. At the moment there is no alternative solvent, acetone is not sufficient, so until an alternative can be developed those industries would have to relocate outside the European Union. 2) Time taken to develop an alternative DMF is relatively new to the acetylene business, but even so it has been known of for more than thirty years. If an alternative was found tomorrow it will take more 10 years to undertake the necessary testing (to achieve approval under European Standard EN1800: Transportable gas cylinders - Acetylene cylinders - Basic requirements, definitions and type testing) followed by the practical evaluation by the end users. The finding of an effective alternative that has lesser risks than DMF is likely to present a major challenge for the industry with a low probability of success. 3) Long life of the equipment being impacted Cylinders in acetylene service have a typical lifetime of 50 or more years, cylinders that are 60,70 or more years old are not unknown. All DMF cylinders in acetylene service are at most fifteen years old. The typical sunset date of 18mths after the addition of the substance to annex XIV is not appropriate to this equipment. If applied then this equipment will have to be scrapped prematurely. The total population of acetylene cylinders in DMF service in Europe is estimated at more than 150 000. 4) Time taken to replace DMF equipment There is limited production capacity for new acetylene cylinders both in the European Union and World Wide (<3% of the total of equipment in service per year). If those cylinders in DMF service had to be replaced tomorrow then the manufacture of the new equipment will take in excess of five years, assuming no other equipment was manufactured. As noted above there is no off the shelf replacement solvent. 5) Limited amount of DMF The use of DMF as a solvent for acetylene cylinders is very small, less than 0.1% of the total DMF used in Europe. The application of review periods based upon major users where the turnover of DMF is quick to a sector where the amount of DMF is minor and the turnover is very slow is inappropriate.	

			On the strategy to manage the risks of DMF: Again Air Liquide Deutschland GmbH, on the basis of its arguments with the review periods, would support the comment made to the Annex XV dossier submission that the risks of DMF should be better managed by the restriction process	
2226	2013/09/17 08:46	Company, Germany	123	-
2170	2013/08/28 12:56	Company, United Kingdom	No comments.	-
2152	2013/08/19 09:59	European Industrial Gases Association (EIGA), Industry or trade association, Belgium	EIGA makes the following comments regarding the review periods 1) Lack of available alternative DMF has certain physical properties which make it necessary for a proportion of the users of acetylene (principally its low vapour pressure which leads to low carryover into the acetylene gas). Historically this was not so important but some industries where the technology has improved require this higher grade and without it they will have to close. If the European Union stops the use of DMF in acetylene service then these industries will have to find an alternative. At the moment there is no alternative solvent, acetone is not sufficient, so until an alternative can be developed those industries would have to relocate outside the European Union. 2) Time taken to develop an alternative DMF is relatively new to the acetylene business, but even so it has been known of for more than thirty years. If an alternative was found tomorrow it will take more 10 years to undertake the necessary testing (to achieve approval under European Standard EN1800: Transportable gas cylinders - Acetylene cylinders - Basic requirements, definitions and type testing) followed by the practical evaluation by the end users. The finding of an effective alternative that has lesser risks than DMF is likely to present a major challenge for the industry with a low probability of success. 3) Long life of the equipment being impacted Cylinders in acetylene service have a typical lifetime of 50 or more years, cylinders that are 60,70 or more years old are not unknown. All DMF cylinders in acetylene service are at most fifteen years old. The typical sunset date of 18mths after the addition of the substance to annex XIV is not appropriate to this equipment. If applied then this equipment will have to be scrapped prematurely. The total population of acetylene cylinders in DMF service in Europe is estimated at more than	Thank you for your comment. Please refer to response to comment 2455 in this section and to response to your comments in the other sections.

			150 000. 4) Time taken to replace DMF equipment There is limited production capacity for new acetylene cylinders both in the European Union and World Wide (<3% of the total of equipment in service per year). If those cylinders in DMF service had to be replaced tomorrow then the manufacture of the new equipment will take in excess of five years, assuming no other equipment was manufactured. As noted above there is no off the shelf replacement solvent. 5) Limited amount of DMF The use of DMF as a solvent for acetylene cylinders is very small, less than 0.1% of the total DMF used in Europe. The application of review periods based upon major users where the turnover of DMF is quick to a sector where the amount of DMF is minor and the turnover is very slow is inappropriate. On the strategy to manage the risks of DMF: Again EIGA, on the basis of its arguments with the review periods, would support the comment made to the Annex XV dossier submission that the risks of DMF should be better managed by the restriction process	
2099	2013/06/25 10:35	Individual, France	no comments	-