

**DECISION OF THE BOARD OF APPEAL
OF THE EUROPEAN CHEMICALS AGENCY**

30 June 2017

*(Substance evaluation – Nanomaterials – Potential risk – Proportionality –
Error of assessment – Article 25)*

Case number	A-014-2015
Language of the case	English
Appellants	Grace GmbH & Co. KG, Germany Advanced Refining Technologies GmbH, Germany
Representatives	David Scannell and Andrew McIntyre Brick Court Chambers, United Kingdom Lydia Duff W.R. Grace and Co., United States of America
Interveners	(I) PETA International Science Consortium Ltd (PISC), United Kingdom (II) ClientEarth, United Kingdom, and Center for International Environmental Law (CIEL), United States of America
Contested Decision	Decision of 11 March 2015 on the substance evaluation of silicon dioxide adopted by the European Chemicals Agency pursuant to Article 46(1) of Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (OJ L 396, 30.12.2006, p. 1; corrected by OJ L 136, 29.5.2007, p. 3; hereinafter the 'REACH Regulation')

THE BOARD OF APPEAL

composed of Mercedes Ortuño (Chairman), Andrew Fasey (Technically Qualified Member and Rapporteur) and Sari Haukka (Legally Qualified Member)

Registrar: Alen Močilnikar

gives the following

Decision

Background to the dispute

1. On the basis of an opinion of the Member State Committee (hereinafter the 'MSC') of the European Chemicals Agency (hereinafter the 'Agency'), and due to initial grounds for concern relating to *'the substance characterisation, nanoparticles and toxicity of different forms of the substance'*, silicon dioxide (CAS No 7631-86-9, EC No 231-545-4) was included in the Community rolling action plan (hereinafter the 'CoRAP') for substance evaluation in 2012 pursuant to Article 44(2) of the REACH Regulation (all references to Articles and Annexes hereinafter concern the REACH Regulation unless stated otherwise). The CoRAP was published on the Agency's website on 29 February 2012. The Competent Authority of the Netherlands was appointed to carry out the evaluation (hereinafter the 'eMSCA').
2. According to the Contested Decision, *'the [eMSCA] has conducted a targeted evaluation that does not include a full evaluation of all elements of the registration dossiers. The evaluation is targeted to the characterisation of the substance, human health hazard assessment in relation to the inhalation route and exposure assessment of the registered synthetic amorphous silica'*.
3. According to the Appellants, synthetic amorphous silica (hereinafter 'SAS') *'is used in hundreds of applications, from coatings, paints, adhesives, rubber, tyres, refrigeration, packaging, metals, refractory, textile, paper, gas drying, petroleum, and refining industries to food, beverage, and related uses. For example, SAS products may be used as free-flow or anti-caking agents in powdered materials [...], or in paper [...], or in rubber and tyres [...]'*.
4. As stated in the Contested Decision, and confirmed during the present proceedings, SAS comprises the following four types: pyrogenic SAS, precipitated SAS, silica gel and colloidal SAS. Annex I to the Contested Decision defines 'SAS types' as *'pyrogenic silica, precipitated silica, silica gel and colloidal silica'*. The Contested Decision also makes a number of references to 'SAS forms' which are defined in Annex I to the Contested Decision as *'all individual size grades and trade names that can be identified separately per SAS type, based on differences in characteristics'*.
5. In their Notice of Appeal, the Appellants state that one of the Appellants *'manufactures and/or imports colloidal, gel and precipitated SAS, as well as small quantities of surface-treated SAS'*; the other Appellant *'imports mixtures containing colloidal and gel SAS. Either Appellant may in the future become involved in the manufacture, import or distribution of other types of SAS'*. The Appellants added at the hearing that they manufacture surface-treated SAS in small quantities, less than one tonne per year. At the hearing the Appellants also confirmed that, although they currently do not manufacture or import pyrogenic SAS, they were registering SAS as a whole and not a sub-set or sub-sets thereof.
6. Pursuant to Article 46(1), the eMSCA prepared a draft decision and, on 27 February 2013, submitted it to the Agency.
7. On 4 April 2013, the Agency sent the draft decision to the Appellants and other registrants of SAS and invited them to provide comments within 30 days pursuant to Article 50(1).
8. By 6 May 2013, registrants of SAS provided comments to the Agency on the draft decision. The draft decision was modified by the eMSCA following these comments.

9. On 29 August 2013, a meeting was held between the eMSCA and some of the registrants of SAS at which the draft decision and the comments thereon were discussed. The participants in that meeting discussed, amongst other things, the findings of a 1991 publication (Reuzel P., Bruijntjes J., Feron V., Woutersen R., '*Subchronic inhalation toxicity of amorphous silicas and quartz dust in rats*', Food and Chemical Toxicology, (1991) 29(5):341-354; hereinafter the 'Reuzel *et al.* publication') describing an inhalation study performed in 1987.
10. On 12 May 2014, a further meeting was held between the eMSCA and some of the registrants of SAS at which the draft decision was discussed.
11. On 4 September 2014, in accordance with Article 52(1), the eMSCA notified the Competent Authorities of the other Member States (hereinafter the 'MSCAs') and the Agency of the modified draft decision and invited them, pursuant to Articles 52(2) and 51(2), to submit proposals for amendment within 30 days.
12. Proposals for amendment were subsequently received from four MSCAs and the Agency.
13. On 10 October 2014, the Agency notified the Appellants of the proposals for amendment and invited them, pursuant to Articles 52(2) and 51(5), to provide comments within 30 days.
14. The eMSCA reviewed the proposals for amendment and further amended the draft decision accordingly (hereinafter the 'amended draft decision').
15. On 20 October 2014, the Agency referred the amended draft decision to the MSC.
16. On 10 November 2014, according to the Contested Decision '*the Registrant(s) provided comments on the proposals for amendment*'.
17. The amended draft decision was discussed at the MSC meeting of 8 to 11 December 2014. At the MSC meeting, representatives of the registrants of SAS presented their views on the proposals for amendment and on the comments of the eMSCA and the Agency. On 11 December 2014, the MSC reached a unanimous agreement on the amended draft decision, as modified at the meeting.
18. The Contested Decision was adopted by the Agency on 11 March 2015 requiring the addressees thereof, including the Appellants, to submit the information set out in paragraphs 19 to 23 below by 20 March 2017.
19. With regards to '*[SAS] (excluding surface-treated forms)*' the Appellants were requested to provide the following information (hereinafter the 'first request'):
 - '1. Information on the following physicochemical properties of each individual SAS form [...] that is manufactured, imported and/or placed on the market, using the indicated test method(s) under standardised conditions that are fully described:
 - (a) The granulometry, which shall include primary particle size, aggregate/agglomerate size, and particle size distribution (number-based). [...];
 - (b) The specific surface area (by volume). [...];
 - (c) The hydroxylation state. [...];
 - (d) The water solubility. [...];
 - (e) The density. [...];
 - (f) The dustiness. [...];
 - (g) The point of zero charge. [...].

The information on the physicochemical properties shall be provided for each individual SAS form covered by the registration of silicon dioxide and shall be provided for the substance forms as produced, processed and placed on the market. Only the Registrant(s) of the substance know the details of each of its forms necessary for their characterisation. Based on this knowledge, they may consider that a test method requested by [the Agency] is not suitable in order to characterise each form of [SAS]. Nevertheless, it is the Registrant(s)' exclusive responsibility 1) to ensure that [the Agency] is in a position to characterise precisely each form of [SAS] and 2) to justify the reasons for the use of another test method instead of a method explicitly required in the present decision.

As an alternative, grouping may be used to provide information on physicochemical properties of SAS forms. In such case the Registrant(s) shall provide a clear justification and documentation as further specified in section III [of the Contested Decision].'

20. With regards to '[SAS] (excluding surface-treated forms)' the Appellants were further requested to provide the following information (hereinafter the 'second request'):

'2. Sub-chronic toxicity study (90-day; OECD 413), in rats via the inhalation route with the following four pyrogenic SAS forms as manufactured that represent:

- i. the lowest specific surface area with the lowest number of hydroxyl groups,*
 - ii. the lowest specific surface area with the highest number of hydroxyl groups,*
 - iii. the highest specific surface area with the lowest number of hydroxyl groups,*
 - iv. the highest specific surface area with the highest number of hydroxyl groups,*
- [...]*

As an alternative, in case for one of the identified forms a sub-chronic toxicity study (90-day, via inhalation) is available (taking into account the modifications to OECD 413 indicated above), and the tested form [...] is fully characterised according to request 1 of this Decision, this information may be provided to cover the information request for this one form.'

21. With regards to '[SAS] (excluding surface-treated forms)' the Appellants were also requested to provide the following information (hereinafter the 'third request'):

'3. Information on the uses of each individual form of SAS [...] that is manufactured, imported and/or placed on the market.'

22. With regards to 'surface-treated SAS' the Appellants were requested to provide the following information (hereinafter the 'fourth request'):

'4. Information on the following physicochemical properties of each individual surface-treated SAS form [...] that is manufactured, imported and/or placed on the market, using the indicated test method(s) under standardised conditions that are fully described:

- a. The granulometry, which shall include primary particle size, aggregate/agglomerate size and particle size distribution (number-based) [...];*
- b. The specific surface area (by volume). [...];*
- c. The hydroxylation state. [...];*
- d. The surface treating agent(s), including chemical identity (IUPAC name and numerical identifiers (CAS and EC)) and type of reaction with the SAS surface;*
- e. The water solubility. [...];*

- f. *The density. [...];*
- g. *The dustiness. [...];*
- h. *The point of zero charge. [...].*

The information on the physicochemical properties shall be provided for each individual surface treated SAS form of silicon dioxide and shall be provided for the substance forms as produced, processed and placed on the market. Only the Registrant(s) of the substance know the details of each of its forms necessary for their characterisation. Based on this knowledge, they may consider that a test method requested by [the Agency] is not suitable in order to characterise each form of the substance. Nevertheless, it is the Registrant(s)' exclusive responsibility 1) to ensure that [the Agency] is in a position to characterise precisely each surface treated form of the substance and 2) to justify the reasons for the use of another test method instead of a method explicitly required in the present decision.

As an alternative, grouping may be used to provide information on physicochemical properties of SAS forms. In such case the Registrant(s) shall provide a clear justification and documentation as further specified in section III [of the Contested Decision].'

23. With regards to 'surface-treated SAS' the Appellants were further requested to provide the following information (hereinafter the 'fifth request'):

'5. All toxicological information on surface-treated SAS as manufactured, imported and/or placed on the market as available to the Registrant(s). This includes all exposure routes, all toxicological endpoints and all forms of surface-treated SAS. Further, a scientific justification shall be provided that substantiates if and why the toxicological information on untreated SAS can be used for safety assessment of surface-treated SAS.'

Procedure before the Board of Appeal

- 24. On 10 June 2015, the Appellants lodged the present appeal at the Registry of the Board of Appeal.
- 25. On 2 September 2015, an application to intervene was received from PISC in support of the Appellants. On the same day, an application to intervene was submitted jointly by ClientEarth and CIEL in support of the Agency.
- 26. On 21 September 2015, the Agency submitted its Defence requesting the Board of Appeal to dismiss the appeal as unfounded.
- 27. By decision of 3 December 2015, the Board of Appeal, having heard the Parties, granted the application to intervene submitted by PISC. On 12 February 2016, having heard the Parties, the Board of Appeal granted the application to intervene submitted by ClientEarth/CIEL.
- 28. On 14 January 2016, the Appellants submitted their observations on the Defence.
- 29. On 31 March 2016, the Agency submitted its observations on the Appellants' observations on the Defence.
- 30. On 29 April 2016, PISC and CIEL/ClientEarth both submitted their statements in intervention.
- 31. On 31 May 2016, the Appellants and the Agency submitted their observations on the statements in intervention.

32. On 3 August 2016, the Parties and the Interveners were notified of the Board of Appeal's decision to close the written procedure.
33. On 4 and 17 August 2016 respectively, the Appellants and the Agency requested that a hearing be held. In view of the Appellants' and Agency's requests, and pursuant to Article 13 of Commission Regulation (EC) No 771/2008 laying down the rules of organisation and procedure of the Board of Appeal of the European Chemicals Agency (OJ L 206, 2.8.2008, p. 5; as amended by Commission Implementing Regulation (EU) 2016/823, OJ L 137, 26.5.2016, p. 4; hereinafter the 'Rules of Procedure'), the Parties were summoned to a hearing which was held on 21 November 2016. At the hearing, the Parties and PISC and ClientEarth/CIEL made oral presentations and responded to questions from the Board of Appeal.

Form of order sought

34. The Appellants, supported by PISC, request the Board of Appeal to annul the Contested Decision in its entirety and order the Agency to refund the appeal fee.
35. PISC requests further that, if the Contested Decision is upheld, the Appellants should be ordered to follow a step-wise approach whereby the physicochemical data is submitted and reviewed before any decision is taken on further animal testing.
36. The Agency, supported by ClientEarth/CIEL, requests the Board of Appeal to dismiss the appeal as unfounded.

Reasons

37. In support of their appeal, the Appellants raise, in essence, five grounds of appeal, which may be summarised as follows.
38. First, the Appellants claim that the Agency materially erred in its assessment of the evidence underlying its decision. In particular, the Agency misinterpreted data and '*placed reliance almost exclusively on one deeply flawed publication*'.
39. Second, the Appellants claim that in its adoption of the Contested Decision the Agency '*failed entirely to consider a number of important and relevant scientific studies brought to its attention by the Appellants and other registrants of SAS*'.
40. Third, the Appellants claim that '*the Agency based its Decision very largely on its own classification of SAS as a "nanomaterial", a classification that the Agency is not empowered to make and that in any event is irrelevant to the toxicity of SAS*'.
41. Fourth, the Appellants claim that the Decision is disproportionate in that it is not appropriate or necessary to achieve the objective of protecting human health and places an unduly heavy burden on the Appellants.
42. Fifth, the Appellants claim that the Agency breached Article 25 by failing to consider whether there were suitable alternatives to vertebrate animal testing.
43. The Board of Appeal notes that by their first, second and third pleas the Appellants argue in effect that the Agency has failed to establish a concern justifying the five requests for information set out in the Contested Decision (see paragraphs 19 to 23 above). The Board of Appeal will first consider these pleas in Section I below, starting with the Appellants' third plea. The Board of Appeal will then examine, in Sections II, III and IV, the Appellants' arguments as they relate to the specific information requirements.

I. The Appellants' pleas alleging that the Agency failed to establish a concern justifying the requests for information

A. The Appellants' third plea, alleging that the Agency unlawfully based its decision on its finding that SAS is a nanomaterial

Arguments of the Parties

44. The Appellants argue that a concern about nanomaterials underlies all five requests for information. The Appellants claim that the Agency has incorrectly used the definition of nanomaterial set out in Commission Recommendation 2011/696/EU on the definition of nanomaterial (OJ L 275, 20.10.2011, p. 38) to justify the imposition of additional and burdensome requirements on the registrants of SAS. Moreover, by characterising SAS as a nanomaterial and seeking to impose additional regulatory requirements on the Appellants on that basis, the Agency has exceeded its competence. The REACH Regulation itself contains no references to nanomaterials and does not empower the Agency to classify substances as nanomaterials pursuant to Commission Recommendation 2011/696/EU.
45. The Appellants claim that the mere fact that the Substance is a nanomaterial within the meaning of the Commission Recommendation 2011/696/EU *'cannot justify any legitimate concern as to the hazardousness of SAS'*. The Appellants argue that the Agency therefore made an error of assessment in using this as a justification for requesting the information.
46. The Appellants claim that there is no evidence to suggest that the presence within a substance of nanomaterials *per se* establishes that the substance is unsafe, hazardous or otherwise presents any danger to human health or the environment. The Appellants claim that this has been confirmed by the Scientific Committee on Emerging and Newly Identified Health Risks (*'Opinion on the scientific basis for the definition of the term "nanomaterial"'*, European Commission, 2010; hereinafter the 'SCENIHR Opinion').
47. The Appellants argue that, in relation to surface-treated SAS, the Agency's Guidance (Questions and Answers: *REACH Registration*, Question 38) clarifies that there is no need to register a surface-treated substance separately from the treated and treating substances, provided that *'any specific hazards or risks of the surface treated substance [are] appropriately covered by the classification and labelling and by the chemicals safety assessment and resulting exposure scenarios'*. Accordingly, surface-treated SAS does not need to be registered as a distinct substance under the REACH Regulation; the specific hazards and risks of surface-treated SAS are addressed in the Chemical Safety Report. The Contested Decision asserts however that the aforementioned Guidance does not apply to SAS because it excludes nanomaterials; nanomaterials were not specifically mentioned *'in any of the documented consultations during the review process'*. The Appellants argue that whilst nanomaterials were not specifically mentioned in the consultation process, this does not mean that they were excluded from the scope of the Guidance; indeed it is more plausible that the absence of a reference to nanomaterials indicated an intention not to treat them differently from other substances.
48. The Agency states that *'although the scientific uncertainty surrounding the potential risks posed by the nanomaterial forms of the substance has triggered the substance evaluation of SAS, this uncertainty alone does not justify the requests for information in the Contested Decision'*. In other words, it is not because SAS is registered in nanomaterial *'forms'* that the Contested Decision has been adopted. According to the Agency, the available data establishes that SAS can be *'suspected to pose a risk'* of toxicity by inhalation.

49. The Agency states that the Contested Decision leaves it to the Appellants to determine whether or not they manufacture or import SAS in any form that fulfils the criteria of the definition of nanomaterials. The Agency states that for the sake of legal certainty the Contested Decision only clarifies the criteria established in the definition in Commission Recommendation 2011/696/EU.
50. The Agency states further in the Defence that the institutions and bodies of the European Union '*unanimously acknowledge that the probability that the minute size of nanoforms of a substance is likely to result in hazardous properties and risks which are specific to these forms, is not hypothetical*'. The Agency argues that the institutions and bodies of the European Union also recognize that knowledge of these '*forms*' is lacking. According to the Agency, '*current scientific knowledge establishes that the risks of nanoforms of substances would require separate assessment. Indeed, the specific hazard potential of nanoforms has been demonstrated by [the SCENIHR Opinion]*'.
51. The Agency states in the Defence that '*registration of a nanomaterial form of a substance has to include all relevant information on that form as manufactured or imported, covering its identity, the properties, uses, effects and exposure related information as well as the relevant classification and labelling, safety assessment and any relevant exposure scenarios. Where this cannot be verified during the detailed assessment of a competent authority of a Member State during substance evaluation, further information may be requested in order to clarify the shortcomings identified*'.
52. The Agency states that the request for all available toxicological information on surface-treated SAS is primarily justified by the SCENIHR Opinion.

Findings of the Board of Appeal

53. The Board of Appeal highlights that, under substance evaluation, in order to establish the necessity of a request for additional information, the Agency must inter alia be able to indicate the grounds for considering that a substance constitutes a potential risk to human health or the environment. The Agency must also be able to demonstrate that the potential risk needs to be clarified, and that the requested measure has a realistic possibility of leading to improved risk management measures (Case A-006-2014, *International Flavors & Fragrances*, Decision of the Board of Appeal of 27 October 2015, paragraph 76).
54. The identification of a potential risk is based on a combination of hazard and exposure information (for example, Case A-005-2014, *Akzo Nobel Industrial Chemicals and Others*, Decision of the Board of Appeal of 23 September 2015, paragraph 61).
55. With regards to exposure to SAS, the Board of Appeal observes that exposure to nanomaterials may be higher than that to substances of a larger molecular size due to their potentially larger surface area, with implications for the reactivity of the substance, and potentially higher dispersion in the environment and in humans.
56. Furthermore, it has not been disputed in the present proceedings that SAS is produced in high volumes. The Contested Decision itself is addressed to over one hundred registrants. At the hearing, the Agency stated that SAS is produced in volumes of over one million tonnes annually. Furthermore, SAS has a wide variety of uses (see paragraph 3 above) leading to considerable human exposure to SAS, both as individuals and as populations. The Board of Appeal notes that, as stated in the Reuzel *et al.* publication, there is also widespread occupational exposure to SAS in a number of industrial settings and through a wide variety of industrial applications.

57. Having established that there is potentially considerable exposure to SAS, the Board of Appeal will examine the Appellants' pleas alleging that the Agency has failed to demonstrate a potential hazard. In this respect the Board of Appeal notes that, in assessing whether there is a potential risk, where there is high potential exposure to a substance the evidence of a potential hazard may be correspondingly less. This approach is consistent with the European Union Courts' interpretation of the precautionary principle, according to which a preventive measure may be taken only if the risk, although the reality and extent thereof have not been 'fully' demonstrated by conclusive scientific evidence, appears nevertheless to be adequately backed up by the scientific data available at the time the measure was taken (judgment of 11 September 2002, *Pfizer Animal Health v Council*, T-13/99, EU:T:2002:209, paragraph 144; see also *International Flavors & Fragrances*, cited in paragraph 53 above, paragraph 77).
58. The Parties agreed, most notably at the hearing, that all 'forms' of SAS covered by the Appellants' registrations are nanomaterials within the meaning of Commission Recommendation 2011/696/EU. References to nanomaterials hereinafter in the present decision are therefore references to nanomaterials within the meaning of Commission Recommendation 2011/696/EU.
59. The Agency acknowledged in the Defence that '*[u]nderstanding the specific properties and any potential risk that may result from the nanomaterial forms of SAS was the triggering interest behind the Substance Evaluation of that substance. It is the explicit reason for which the Dutch authorities suggested SAS for inclusion in the CoRAP list*'.
60. The Agency explained in the Defence that the fact that SAS is a nanomaterial is not used to justify the requests for information in the Contested Decision. The Agency stated that '*the Contested Decision is justified mainly by the fact that the findings of an inhalation study resulted in considering that at least one type of SAS is "suspected of posing a risk"*'.
61. The Board of Appeal observes however that the Agency's submissions, and the Contested Decision, are not entirely consistent in this regard and in part suggest that the fact that SAS is a nanomaterial may be sufficient to demonstrate a potential hazard. For example, the Agency stated during the present proceedings that '*[g]iven the scientific uncertainties on the causal links between the minute sizes of nanomaterials and the toxicity of the substance concerned, as well as the indication of divergence of the physicochemical properties reflected in the dossier of SAS, there is a real information need to ensure the safe use of the substance in all of its forms*'. The Agency also stated that '*[t]he scientific uncertainty surrounding nanomaterial forms of substances, in general, raises concerns that merit further regulatory attention*'.
62. Nonetheless, the Board of Appeal understands from the Contested Decision and the written and oral submissions in the present case (see for example paragraph 48 above) that the Agency does not use the fact that a substance is a nanomaterial on its own to establish a concern. In other words, the Agency does not ask for information on nanomaterials exclusively on the grounds that they are nanomaterials.
63. The Agency's position in the present case is therefore that there were specific grounds for concern beyond SAS being a nanomaterial. This is implicitly acknowledged by the Appellants in the Notice of Appeal in stating that the Reuzel *et al.* publication '*underpins all five of the Requests. Significant reliance is placed on the conclusions reached in this publication. Indeed, the Reuzel publication appears to be the only scientific paper on the toxicity of SAS on which the Agency places reliance*'.

64. In light of the above, the Board of Appeal finds that the fact that SAS is a nanomaterial was clearly a major factor in adding silicon dioxide to CoRAP but is not the sole reason SAS was considered, pursuant to substance evaluation, to pose a potential risk for human health or the environment.
65. The Board of Appeal further finds that being a nanomaterial is insufficient on its own to justify a potential concern under substance evaluation. The Board of Appeal notes that some nanomaterials are hazardous whilst others are not. Nanomaterial is a categorisation of a substance by its size. However, the fact that a substance is a nanomaterial neither implies a specific risk nor does it necessarily mean that the substance has different hazard properties compared to its non-nano 'form'. Furthermore, no consistent causal link has yet been established between size and hazardous properties. The Board of Appeal further notes that the definition of nanomaterials establishes a size threshold for substances to be nanomaterials. The definition does not however mean that substances below the threshold are *per se* more hazardous than those above this threshold. The Board of Appeal notes that in the present case the Contested Decision is justified by the Reuzel *et al.* publication and its findings with regards to the inhalation toxicity of SAS and not only on the basis that SAS is nanomaterial.
66. In light of the above, the Appellants' claim that the Contested Decision should be annulled on the grounds that all requests for information are based on irrelevant considerations, that is the Agency's request for information is based on its finding that SAS is a nanomaterial, is dismissed as unfounded.
67. The Board of Appeal will next examine together the other pleas related to the alleged lack of concern, namely the Appellants' first plea, alleging a manifest error of assessment, and the Appellants' second plea, alleging the Agency's failure to consider relevant material.

B. The Appellants' first plea, alleging a manifest error of assessment and second plea, alleging a failure to consider relevant material

Arguments of the Parties

68. The Appellants claim that the Reuzel *et al.* publication underpins all five information requests in the Contested Decision. The Appellants add that although the Agency refers to other studies in the Contested Decision, in reality it gave little weight to those studies.
69. The Appellants argue that there are a large number of papers addressing the toxicity of SAS which it brought to the Agency's attention either at the time that SAS was registered or in the course of the substance evaluation procedure. The weight-of-evidence casts serious doubt on the reliability of the Reuzel *et al.* publication. The Appellants claim further that the Agency failed to consider all the available information.
70. The Appellants state that, despite indications to the contrary in the Contested Decision, the Reuzel *et al.* publication does not demonstrate '*differences in toxicity between forms of SAS*'. The Appellants add that the Reuzel *et al.* publication '*investigated potential differences between types of SAS, and between surface-treated and non-surface treated pyrogenic SAS. It did not investigate differences between forms*'.
71. The Appellants claim that the results described in the Reuzel *et al.* publication, which was based on an inhalation study on rats, represent typical inflammatory reactions of the rat lung to high particle loads and do not indicate any potential danger to human health. According to the Appellants, the effects observed in the Reuzel *et al.* publication

were not specific to SAS but rather resulted from lung or particle overload. The Appellants argue that the Agency exaggerated the severity of the adverse effects observed in the Reuzel *et al.* publication, which are in any case reversible.

72. The Appellants claim that, in relation to the first (see paragraph 19 above) and fourth (see paragraph 22 above) requests, there is no specific link between the physicochemical properties identified in these requests and the toxicity of SAS. In particular, the Reuzel *et al.* publication '*does not purport to show any correlation or relationship between toxicity and any of the seven physicochemical characteristics identified in the first request*'. The Appellants also argue that the Agency does not explain how the physicochemical data requested could lead to improved risk management measures.
73. The Appellants claim that the existing studies made available to the Agency and the eMSCA found no evidence for a fibrogenic effect of SAS in the human lung. According to the Appellants, the Agency has not therefore demonstrated a risk to human health or the environment that may occur in reality. In particular, the Appellants refer to the '*Cross-sectional study on respiratory morbidity in workers after exposure to synthetic amorphous silica at five German production plants*' (Morfeld (2013); hereinafter the 'Morfeld study') and a report by the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (hereinafter the 'MAK-Commission') of the *Deutsche Forschungsgemeinschaft* (German Research Foundation).
74. The Appellants argue that, in any case, the Agency has not presented any basis at all on which the non-pyrogenic types of SAS might be said to pose a potential risk to human health or the environment. Consequently, insofar as the Contested Decision requires the Appellants to provide information on precipitated, colloidal and gel SAS, it is entirely unfounded and unlawful.
75. The Appellants also claim that the Agency has not demonstrated that surface-treated SAS poses a potential risk of toxicity justifying the fourth (see paragraph 22 above) and fifth (see paragraph 23 above) requests in the Contested Decision. The Agency also failed to consider the evidence made available by the Appellant. The Appellants argue that, in any case, the Agency is not competent to request information on surface-treated SAS as the Appellants do not manufacture or import surface-treated SAS in a quantity that would require registration under the REACH Regulation.
76. The Agency claims that '*there is only one relevant key study with respect to the toxic properties of pyrogenic silica*', namely the Reuzel *et al.* publication. The Agency claims that the other studies presented by the Appellants refer to other types of SAS and that these therefore cannot change the findings of the Reuzel *et al.* publication.
77. The Agency states that the Contested Decision is justified mainly by the fact that the findings of the Reuzel *et al.* publication indicate that at least one type of SAS is suspected of posing an inhalation toxicity concern. The Agency states that this finding is based on an evaluation of all the available data.
78. The Agency accepts that the Reuzel *et al.* publication does not explicitly refer to '*forms*' of SAS. The Reuzel *et al.* publication was performed on commercial products representing different SAS types. These commercial products are in practice forms of different types of SAS. The Agency adds that the Reuzel *et al.* publication indicates that the various types of SAS can differ in toxicity. Based on the results of this publication and the lack of data comparing the toxicity of different types of SAS and the different forms of pyrogenic SAS, it is reasonable to believe that at least the pyrogenic type of SAS is suspected to pose a risk of toxicity. A specific study is therefore necessary to

confirm this risk and to verify the extent to which it may also concern other forms of pyrogenic SAS.

79. The Agency states in the Defence that *'based on current evidence there is no reason to believe that there was impaired clearance and particle retention that would have led to lung overload. Instead, it is highly unlikely that the fibrosis observed in the Reuzel study is due to particle overload'*.
80. The Agency states that, although the severity of fibrosis decreased during the recovery period, fibrosis was still evident 52 weeks after the end of exposure and was therefore not fully reversible. The Agency argues further in the Defence that even a reversible effect may be relevant and that *'reversibility may not be applicable for persons that are continuously exposed to SAS such as workers who may be exposed on a weekly basis during many years'*.
81. The Agency claims that it and the eMSCA took the Morfeld study into account. The eMSCA and the Agency considered however that this study did not disprove the findings of the Reuzel *et al.* publication. The Agency argues for example that *'former workers that are retired or have quitted their job (e.g., due to health problems) are not included in the study group. This may have introduced an unknown bias in the study populations and may have introduced the so-called "healthy-worker effect"'*. In addition, the Agency raises doubts regarding the use of cumulative exposure levels as the study does not take into account the intensity of exposure which may be of greater importance than the duration. The Agency also highlights that the Morfeld study, in which nearly half of the examined workers were exposed to precipitated SAS and the others to pyrogenic SAS, does not clearly distinguish between exposures to each.
82. The Agency considers that the Morfeld study did not investigate the effects on lungs or other organs of the workers following exposure to SAS and, as a result, in toxicological terms, no dose/response has been described. The Agency adds that *'the conclusions that (all forms of) SAS [have] no or only a minor effect on lung function, can therefore not be endorsed'*. The Agency also argues that *'as most critical effects make it plausible that during longer exposure there may be effects on the lungs which should be further investigated [...]'. The Morfeld survey is not suitable to change this conclusion as these specific effects were not covered by the survey'*.
83. The Agency states that the MAK-Commission conclusions were introduced for the first time during the present appeal proceedings and that they were not discussed during the substance evaluation process. The Agency argues however that the MAK-Commission conclusions do not disprove the findings in the Contested Decision. The Agency also argues that the information from the MAK-Commission is outdated, dating back to 1991, and in any case may simply demonstrate a difference of scientific opinion.
84. The Agency claims that the concern which justifies the request for information on surface-treated SAS can be found in the Reuzel *et al.* publication and the conclusions of the SCENIHR Opinion. In particular, the Agency argues that the differences in toxicity observed in the Reuzel *et al.* publication for different types of SAS show that surface-treatment can considerably alter the toxicity of an SAS type or form. The Agency also states that *'the potential risk that surface-treated forms of SAS have different toxic effects, is not limited to inhalation toxicity, but may occur for any type of toxicity. This risk exists potentially for all toxicity endpoints which do not contain studies concerning at least one surface treated form of SAS and other surface-treated forms or non-treated forms. It is only in case where the testing material differs in terms of surface treatment*

that a difference may occur. In any other case, the potential risk of difference of effect cannot be observed'.

85. The Agency also states that, according to the SCHENIR Opinion, each combination of a nanomaterial and a coating has to be considered as an individual case. The Agency argues that this finding is echoed in the Reuzel *et al.* publication which shows differences in effects between surface-treated 'forms' and non-surface-treated 'forms' of SAS.

Findings of the Board of Appeal

86. The Appellants claim that the Contested Decision should be annulled on the ground that the Agency committed an error of assessment in interpreting the results of the Reuzel *et al.* publication as justifying the requests for further data under substance evaluation. The Appellants also claim that the Agency failed to consider all the available information which shows that SAS is not hazardous under anticipated conditions of use.
87. When examining whether the Agency has made an error of assessment, the Board of Appeal must examine whether the Agency has examined, carefully and impartially, all the relevant facts of the individual case which support the conclusions reached (Case A-017-2014, *BASF*, Decision of 7 October 2016, paragraph 74 and the case-law cited therein).
88. The Contested Decision requests information on the four types of SAS, namely pyrogenic SAS, precipitated SAS, silica gel and colloidal SAS. The Contested Decision also requests information on 'each individual surface-treated SAS form'.
89. The Board of Appeal, having established an exposure concern (see paragraph 55 and 56 above), will examine in turn the arguments related to the potential hazard of (1) non-surface treated precipitated SAS, silica gel and colloidal SAS; (2) non-surface treated pyrogenic SAS; and (3) surface-treated SAS.

1. Potential concern of non-surface treated precipitated SAS, silica gel and colloidal SAS

90. Based primarily on the findings of the Reuzel *et al.* publication, the Agency concluded that, at least, pyrogenic SAS posed a potential inhalation toxicity concern that required further examination. The Agency also contends that the unexplained differences in toxicity between different types of SAS observed in the Reuzel *et al.* publication is in itself a potential concern that needs to be clarified.
91. The Reuzel *et al.* publication reports on a thirteen-week inhalation study, followed by post-exposure observation of up to one year, on three commercial products, which are examples of pyrogenic SAS, surface-treated pyrogenic SAS and precipitated SAS. Samples of silica gel, colloidal SAS and other surface-treated types of SAS were not tested. The Reuzel *et al.* publication states that '*[o]f the amorphous silicas examined [the example of pyrogenic SAS tested] induced the most severe changes in the lungs, which only partly recovered, whereas [the example of precipitated SAS tested] induced the least severe, completely reversible lung changes'.*
92. The Contested Decision seems to acknowledge that there is a concern for inhalation toxicity with regards to pyrogenic SAS only:
- 'This is in line with the findings in various other repeated dose inhalation studies available in the registration dossiers that indicate that fibrosis is only associated with exposure to pyrogenic SAS [...]'.*

93. The Board of Appeal also observes that whilst the Contested Decision seeks to demonstrate, in particular through the Reuzel *et al.* publication, that pyrogenic SAS presents a potential hazard for inhalation toxicity, there is little evidence in the Contested Decision to demonstrate that the other three types of SAS, namely precipitated silica, silica gel and colloidal silica, present a potential hazard that needs to be clarified.
94. This observation is supported for two of the types – precipitated SAS and silica gel – in the Contested Decision itself which states that:
- '[n]o fibrosis was observed in any of the available inhalation studies with precipitated SAS or silica gel, apart from the single finding by Reuzel et al. (1991) for [the example of precipitated SAS tested].'*
95. In its Defence, the Agency states that:
- '[t]he "suspected risk" addressed in the Contested Decision is related to pyrogenic SAS, which is according to the current understanding of [the Agency] the most toxic/potent SAS type. The available information shows that the other three types of SAS - precipitated SAS, silica gel and surface treated SAS - have different or less toxicity properties than pyrogenic SAS and therefore cannot be compared. There is only one relevant key study with respect to the toxic properties of pyrogenic silica (i.e. Reuzel study). The references of the Appellants to other studies and/or publications are therefore not able to change this finding.'*
96. The Agency confirmed in its Defence that:
- '[the] request for toxicological information is limited to the SAS type, which according to the findings of the Reuzel study is "suspected of posing a risk". Accordingly, the Contested Decision is restricted to the pyrogenic type of SAS, which needs to be further investigated in order to clarify the existence of an actual concern'.*
97. The Board of Appeal observes that there is no examination in the Contested Decision as to whether colloidal SAS presents a potential concern. In its Notice of Appeal, in claiming that there is no concern for colloidal SAS, the Appellants refer to the Warheit (1991) study which, according to the Appellants, showed *'no observable effects in rats exposed to 10 mg/m³ colloidal silica in a 28-day inhalation study. At higher doses most biochemical parameters returned to control values following a 3-month recovery period'*.
98. In the Defence the Agency seems to confirm that there is no concern for colloidal SAS based on the available evidence. In response to the Appellants' arguments in the Notice of Appeal, the Agency states that *'from the information that is available in the dossier, there are as yet no indications that colloidal silica induces fibrosis, therefore further studies were requested on forms of pyrogenic silica and the reference to this study does not help in clarifying the concern identified for Silicon dioxide as pyrogenic SAS'*.
99. In view of paragraphs 91 to 98 above, the Board of Appeal finds that the Agency has not demonstrated that precipitated SAS, silica gel and colloidal SAS present a hazard concern that would justify the requests for information set out in the Contested Decision.
100. The Agency however also argues that the information requested in the Contested Decision is justified by the fact that the Reuzel *et al.* publication and the information available in the Appellants' registration dossiers does not explain the difference in toxicity between the four different types of SAS. In this regard, the Contested Decision states that:

'The available inhalation studies indicate differences in toxicity and potency between different types of SAS, with pyrogenic SAS showing a higher toxic potential than precipitated SAS and silica gel. These differences in potency between SAS types are inextricably bound up with differences in physicochemical characteristics. Physicochemical properties vary significantly between SAS types, but also between different SAS forms within one SAS type [...]. Considering this dependency of toxicity on physicochemical characteristics, identification of the individual forms of SAS for their physicochemical characteristics is required. [...]

The need for individual characterisation of all registered forms is further emphasised by the fact that both the mammalian and environmental toxicology of SAS are significantly influenced by their physicochemical properties [...]. Differences in toxicity between forms of SAS have been demonstrated by Reuzel et al. (1991)'.

101. The Board of Appeal finds, however, that the Agency has not substantiated its argument that *'differences in potency between SAS types are inextricably bound up with differences in physicochemical characteristics'* and that the potential concern established in the Reuzel *et al.* publication for pyrogenic SAS therefore extends to other types of SAS.
102. The Agency has explained in the Contested Decision that it would like to examine how the physicochemical properties of *'forms'* and types of SAS affect their toxicity. In principle, the Board of Appeal observes that this could be a legitimate objective of a substance evaluation decision. However, the decision in question would have to clearly establish how the physicochemical data requested would be used, in conjunction with any available data and new hazard testing, to clarify the identified potential concern. For example, a testing programme might be established to identify the physicochemical characteristics that are the drivers of toxicity for a particular substance. In this particular case, however, there is no clear indication as to how the extensive data requested on the physicochemical parameters of all *'forms'* of SAS would be used, in conjunction with available data and/or the inhalation toxicity testing requested on pyrogenic SAS, to identify the drivers of toxicity or show how the different physicochemical properties of types or *'forms'* of SAS affect their toxicity. In short, a considerable amount of data is requested but it has not been explained how these data will be used to meet the objectives pursued.
103. In view of the above, the Board of Appeal considers that the Agency has not demonstrated a potential concern with regards to precipitated SAS, silica gel and colloidal SAS that would justify the first and third requests. The Appellants' arguments that the Agency committed an error of assessment by failing to examine carefully and impartially all the relevant facts of the case must therefore be accepted.
104. The Board of Appeal recalls that the requests for information on precipitated SAS, silica gel and colloidal SAS concern the first and third requests as the second request concerns pyrogenic SAS only and the fourth and fifth requests concern surface-treated SAS. As a result, the first request and the third request must be annulled in so far as they concern precipitated SAS, silica gel and colloidal SAS.
105. The Board of Appeal will next examine the Appellants' arguments in support of their contention that the Contested Decision, in particular through its reliance on the Reuzel *et al.* publication, does not demonstrate that pyrogenic SAS presents a potential risk of inhalation toxicity.

2. Potential concern of non-surface treated pyrogenic SAS

106. The Board of Appeal observes that in Section III of the Contested Decision, in relation to the first request, under the heading '*Justification why new information is needed*', the Agency cites a study by Johnston *et al.*, '*Pulmonary chemokine and mutagenic responses in rats after sub-chronic inhalation of amorphous and crystalline silica*', Toxicological Sciences 56 (2000) 405-413 (hereinafter the 'Johnston *et al.* study'). The Contested Decision states with regards to that study that '*rats were exposed to [the example of pyrogenic SAS tested] for 13 weeks at a concentration of 50 mg/m³. Histopathology data revealed fibrosis in the alveolar septae, which subsided during a recovery period (≥ 3 months)*'.
107. The Board of Appeal finds that, whilst relevant to the consideration of the inhalation toxicity of pyrogenic SAS, the Johnston *et al.* study was performed at high doses and, on its own, constitutes weak evidence of a potential inhalation toxicity concern for pyrogenic SAS.
108. The same section of the Contested Decision also refers to other studies:
'Further, signs of (collagenic) fibrosis were observed by Groth et al. (1981), Klosterkötter (1969) and Schepers et al. (1957a, 1957b), although the reliability of some of the results was questioned and doses were relatively high'.
109. The Board of Appeal also concludes that, whilst relevant to the consideration of the inhalation toxicity of pyrogenic SAS, as these studies have questions over their reliability and were also performed at relatively high doses they, on their own, also constitute weak evidence of a potential concern.
110. Nonetheless, although the results of the studies mentioned in paragraphs 106 and 108, on their own, constitute weak evidence of a potential inhalation toxicity concern with regards to pyrogenic SAS, they do not demonstrate the absence of a concern. It is therefore clear that the findings of the Reuzel *et al.* publication are crucial in determining whether there is a potential concern with regards to the inhalation toxicity of pyrogenic SAS that needs to be clarified. The Agency itself states in the Defence that '*[t]here is only one relevant key study with respect to the toxic properties of pyrogenic silica (i.e. Reuzel study). The references of the Appellants to other studies and/or publications are therefore not able to change this finding*'.
111. The Board of Appeal will therefore examine the Appellants' arguments (see paragraphs 68 to 75 above) that the Reuzel *et al.* publication does not support the Agency's contention that pyrogenic SAS presents a potential inhalation toxicity concern.
112. In response to the Appellants' argument that the Agency exaggerated the severity of the adverse effects observed in the Reuzel *et al.* publication, the Board of Appeal notes that the Reuzel *et al.* publication states, *inter alia*, that:
'Of the amorphous silicas examined [the example of pyrogenic SAS tested] induced the most severe changes in the lungs, which only partly recovered, whereas [the example of precipitated SAS tested] induced the least severe, completely reversible lung changes'.
113. The findings in the Contested Decision are consistent with those reported in the Reuzel *et al.* publication. For example, the Contested Decision reflects the view that the results were more severe in the pyrogenic SAS tested than in the other types of SAS tested. In this respect, the Contested Decision states that '*the study revealed that 30 mg/m³ [of*

the example of pyrogenic SAS tested] induced more severe changes in the lungs as compared to 30 mg/m³ [of the example of precipitated SAS tested]’.

114. The Board of Appeal therefore finds that the Appellants have not demonstrated that the Agency exaggerated the results of the Reuzel *et al.* publication. Furthermore, the Board of Appeal finds that the Reuzel *et al.* publication does indicate adverse effects with regard to the inhalation toxicity of pyrogenic SAS.
115. The Board of Appeal will next examine the Appellants’ arguments related to (i) the claim that the results indicating fibrosis were caused by particle overload, (ii) the claim that any adverse effects were reversible after a period of recovery, and (iii) the claim that the studies made available to the Agency show that there is no evidence of fibrosis in the human lung after exposure to SAS. By all of these arguments the Appellants claim, in essence, that the Agency failed to take into account all the information available to it and failed to establish a concern.

(i) The Appellants’ claim that the effects observed in the Reuzel et al. publication are caused by particle overload

116. The Appellants claim that any adverse effects, including fibrosis, reported in the Reuzel *et al.* publication are due to particle, or lung, overload, in other words that the effects observed resulted from chronic exposure to high concentrations of particles rather than to SAS. The Board of Appeal observes that this issue was raised during the decision-making procedure, most notably by way of an expert opinion provided to the Agency, and that these views were addressed in the Contested Decision in several places. For example, the Contested Decision states that:

‘Considering the much higher incidence of fibrosis following exposure to [the example of pyrogenic SAS tested] as compared to [the example of precipitated SAS tested] and [the example of surface-treated pyrogenic SAS tested], and the fact that fibrosis occurs already at low exposure concentrations of [the example of pyrogenic SAS tested], the fibrosis cannot be attributed to just a particle (over)load of the lungs. This is further substantiated by the fact that Reuzel et al. (1991) reported lower silicon content in the lung of rats exposed to [the example of pyrogenic SAS tested] than in the lung of rats exposed to the other SAS forms; the silicon clearance from the lung appeared to be faster in [the example of pyrogenic SAS tested] exposed rats’.

117. The Contested Decision also states that:

‘The observed fibrosis cannot just be attributed to the number of SAS particles for the following reasons:

1. Fibrosis is already observed at 1 mg/m³ pyrogenic SAS (the lowest concentration tested), but not at exposure to 30 mg/m³ of precipitated SAS or surface-treated pyrogenic SAS, although the number of particles will have been considerably higher in the latter two exposures.

2. Lung silicon content is lowest for pyrogenic SAS as compared to the other two SAS types tested. All three types had similar exposure concentrations of approximately 30 mg/m³.

Reuzel et al. (1991) measured the total amount of Si in the lungs. The results showed that silicon levels were lowest for [the example of pyrogenic SAS tested], in comparison to [the example of precipitated SAS tested] and [the example of surface-treated pyrogenic SAS tested]. Further, [the example of pyrogenic SAS tested] was quickly cleared from the lungs; no or only minimal levels were detected at 13 weeks post

exposure and longer. Si levels in rats treated with [the example of precipitated SAS tested] and [the example of surface-treated pyrogenic SAS tested] were still detected at 39 weeks post exposure.

If the fibrosis would have been solely caused by a high particle load, pulmonary fibrosis would also have been expected in rats exposed to [the example of precipitated SAS tested], for which significantly higher Si levels in the lung were observed than for [the example of pyrogenic SAS tested]. The lung silicon contents for [the example of pyrogenic SAS tested] and [the example of precipitated SAS tested], as observed in the Reuzel et al. (1991) study, therefore support the conclusion that the fibrosis is not caused by particle overload but is specific for [the example of pyrogenic SAS tested]. Further, fibrosis was already observed at low levels of 1 mg/m³ and 6 mg/m³ [of the example of pyrogenic SAS tested]. These data altogether suggest that it is highly unlikely that pulmonary fibrosis in rats exposed to [the example of pyrogenic SAS tested] is the result of particle overload.'

118. The Board of Appeal has considered the arguments made by both Parties and, in light of the considerations quoted above, comes to the conclusion that the Agency has taken into account the Appellants' claims that the results observed in the Reuzel *et al.* publication are due to particle overload and are therefore not indicative of toxicity. The Board of Appeal finds that the Appellants have not shown that the Agency has committed an error in its assessment by failing to consider carefully and impartially all the relevant facts of the individual case which support the conclusions reached.
119. At the hearing the Appellants claimed that the '*Results of a PWG (pathology working group) review of the Reuzel et al. publication (1987)*' (hereinafter the 'PWG review') dated 16 June 2016, which was submitted in another appeal against the same Contested Decision (Case A-015-2015, *Evonik Degussa and Others*), should also be considered by the Board of Appeal in the present case. The Appellants state that this is the case despite the fact that the Appellants were unable to submit the PWG review in the present case due to issues related to ownership of that document. Without deciding on whether the Board of Appeal was required to take into account a document not submitted by the Parties in the present case, in paragraph 173 of its Decision of 30 June 2017 in Case A-015-2015, *Evonik Degussa and Others*, the Board of Appeal highlighted that the PWG review:

'...it is not a new experimental study, but rather the opinion of experts formed on the basis of a re-evaluation of an existing experimental study. The Board of Appeal finds that whilst the PWG review provides further valuable insight into the results of the 1987 Reuzel et al. study it is not capable of answering the potential concern identified with regards to pyrogenic SAS in the Contested Decision. The issues raised in the PWG review regarding fibrosis, reversibility and particle overload have already been examined in the Contested Decision and during the substance evaluation process. As a result, the conclusions of the PWG review do not affect the Board of Appeal's findings.'
120. It follows that even if the PWG review had been submitted by the Appellants in the present appeal, it would not have altered the Board of Appeal's findings with regard to lung or particle overload.
121. As a general remark, the Board of Appeal notes that the data available for substance evaluations is in some cases inconsistent or indeed contradictory and in others leaves questions open. It is therefore not surprising that there is often a difference of opinion between experts when assessing the available data. The Board of Appeal notes that one of the main purposes of substance evaluation is to clarify potential concerns and thereby

help resolve the differences of opinions between experts and in others to clarify a concern over which there is a consensus. The testing or information required pursuant to a substance evaluation should be specifically designed to clarify potential concerns taking into account all available information. In this particular case, whilst the Appellants have clearly shown why they disagree with the conclusion reached by the Agency with regards to the potential inhalation toxicity concern, in light of the evidence regarding particle overload, the Board of Appeal finds that the Appellants have not shown that the Agency's conclusion that there is a potential concern is incorrect.

(ii) *The Appellants' claim that any adverse effects observed in the Reuzel et al. publication were reversible*

122. The Reuzel *et al.* publication states that:

'Although [the example of pyrogenic SAS tested] was very quickly cleared from the lungs and regional lymph nodes, the changes in these organs were only partly reversed during the post-exposure period in rats exposed to 30 mg/m³. [The example of surface-treated pyrogenic SAS tested] and the lower levels of [the example of pyrogenic SAS tested] resulted in less severe, and mostly reversible, changes. [...]

Of the amorphous silicas examined [the example of pyrogenic SAS tested] induced the most severe changes in the lungs, which only partly recovered, whereas [the example of precipitated SAS tested] induced the least severe, completely reversible lung changes'.

123. The Board of Appeal observes that the Arts *et al.* study (2007) (Arts JH, Muijser H, Duistermaat E, Junker K, Kuper CF, *Five-day inhalation study of three types of synthetic amorphous silicas in Wistar rats and post-exposure evaluations for up to 3 months*, Food and chemical toxicology, 2007 Oct; 45(10):1856-67), which was submitted by the Appellants to support their contention that the effects are reversible, is a five-day study conducted on rats using different concentrations of precipitated SAS, silica gel and pyrogenic SAS. The Board of Appeal finds that these short-term studies cannot reliably answer the potential inhalation toxicity concern, and the possible reversibility of effects, following long-term exposure.

124. The Board of Appeal notes that, with regards to pyrogenic SAS, the Reuzel *et al.* publication did not demonstrate that the adverse effects observed, i.e. fibrosis, were in all cases fully reversible. The inhalation toxicity study requested in the Contested Decision should help to clarify this issue with regards to pyrogenic SAS. The Board of Appeal observes that requesting further information to clarify the potential inhalation toxicity concern, including the reversibility of effects, is consistent with the aims of substance evaluation.

125. For the reasons stated in paragraphs 119 above, the conclusions of the PWG review do not affect the Board of Appeal's findings with regard to the reversibility of effects.

126. The Appellants' arguments on the reversibility of effects must therefore be dismissed.

(iii) *The Appellants' claim that the studies made available to the Agency show that there is no evidence of fibrosis in the human lung after exposure to SAS*

127. The Morfeld study was submitted to the eMSCA only on 17 December 2013 which is after the draft decision was notified to the Appellants. The Agency argues that it nevertheless did take the study into account in the Contested Decision and has

explained, in these proceedings, why it considers that this study does not clarify the concern with regards to inhalation toxicity for pyrogenic SAS.

128. Whilst the Appellants have indicated why they find the evidence in the Morfeld study to be persuasive, the Board of Appeal does not accept that the Morfeld study sufficiently addresses and clarifies the potential inhalation toxicity concern regarding pyrogenic SAS. Indeed, the conclusions to the Morfeld study itself states that the methods used in the study '*suffer from considerable uncertainties that need to be considered in epidemiological studies.*' The Board of Appeal finds that in light of the lack of a dose/response assessment, and the lack of clarity as to exactly what the workers were exposed to and for how long, the Morfeld study does not clarify the identified concern, namely inhalation toxicity, with regards to pyrogenic SAS and cannot therefore refute the conclusions reached in the Contested Decision.

(iv) Conclusion on the potential concern regarding non-surface treated pyrogenic SAS

129. In light of the above, the Board of Appeal finds that the Agency has established a potential concern with regards to inhalation toxicity for pyrogenic SAS. The studies and expert opinions identified by the Appellants do not answer this concern nor do they show that the Agency made an error of assessment. Therefore, the evidence of a potential inhalation toxicity concern, taken in conjunction with the widespread exposure potential (see paragraphs 55 to 56 above), means that the Agency did not make an error of assessment in concluding that there is a potential risk for inhalation toxicity with regards to pyrogenic SAS.
130. The Appellants' arguments that, with regards to pyrogenic SAS, the Agency failed to apply a weight-of-evidence approach and committed an error of assessment in interpreting the results of the Reuzel *et al.* publication must therefore be dismissed as unfounded.
131. The Board of Appeal will next examine whether the Agency has demonstrated a potential concern for surface-treated SAS that needs to be clarified pursuant to substance evaluation.

3. Potential concern of surface-treated SAS

132. According to the Contested Decision '*[a]s surface treatment may affect the characteristics of the registered substance, an underestimation of the hazards cannot be excluded based on the available data*'. The Contested Decision states further that the grounds for concern can also be found in a '*generic concern raised in the SCENIHR Opinion*'. According to the SCENIHR Opinion:

'Purposely applied and environmentally acquired coatings can have a major impact on nanomaterial interaction with biological systems. The coating and core together control the properties of a given nanomaterial and it is not useful to look at either the properties of the core or the coating in isolation as they may not be representative of how the nanomaterial will behave in a given environment. Thus, each combination of a nanomaterial and a coating has to be considered as an individual case when safety evaluation of a specific nanomaterial is considered'.

133. The Board of Appeal has found that the Reuzel *et al.* publication demonstrates a potential concern with regards to pyrogenic SAS only (see paragraphs 86 to 131 above). According to the Reuzel *et al.* publication, the surface-treated '*form*' of pyrogenic SAS tested at a level of 30 mg/m³ induced similar but generally less severe changes than

the non-surface treated 'form' of pyrogenic SAS tested at the same level. Furthermore, these changes largely disappeared during the recovery period. In the absence of any other specific evidence related to surface-treated SAS, the Board of Appeal finds that this evidence is insufficient to justify further testing to clarify a potential inhalation toxicity concern with regards to surface-treated SAS. The Agency's argument that the requests for information on surface-treated SAS are justified by the Reuzel *et al.* publication must therefore be dismissed. The Board of Appeal notes that the results of any inhalation toxicity testing on pyrogenic SAS may give rise to, or contribute to the evidence of, a potential concern for surface-treated pyrogenic SAS.

134. With regards to the Agency's reliance on the SCENIHR Opinion, the Board of Appeal observes that those conclusions are not specific to SAS but to surface-treated nanomaterials in general. The SCENIHR Opinion also states that not all nanomaterials pose a risk to human health and the environment. Furthermore, the SCENIHR Opinion states that coatings 'can' have an impact on nanomaterials and that the properties of the coating 'may not be representative'. The Board of Appeal finds therefore that, as with the alleged general concerns related to nanomaterials (see paragraphs 59 to 67 above), the Agency cannot rely on a general concern regarding surface-treated substances that are also nanomaterials. The Agency must be able to demonstrate a specific concern in relation to the substance at issue.
135. In addition, in justifying the grounds for concern, the Agency stated in the Defence that 'the Appellants have provided no information enabling the identification or the nature of surface-treatment, no information explaining the Reuzel findings in that respect, and no experimental data demonstrating the absence of difference in toxicity between surface-treated and non-surface-treated form of SAS'. This, however, indicates an absence of information only. The Agency must be able to demonstrate a specific concern that needs to be clarified and how the information and/or testing required will help to clarify that concern (see paragraph 53 above).
136. The Board of Appeal finds therefore that the Agency has failed to identify a potential concern with regards to surface-treated SAS. The fourth and fifth requests, which specifically concern surface-treated SAS, are therefore annulled in their entirety.

4. Conclusion on the existence of a concern for SAS

137. In paragraphs 90 to 104 above the Board of Appeal has found that the Agency failed to establish a potential concern in relation to precipitated SAS, silica gel and colloidal SAS. The Contested Decision has therefore been annulled in so far as it requests additional information on these types of SAS. For the same reason the Contested Decision has been annulled in so far as it requests information on surface-treated SAS (see paragraphs 132 to 136 above). The Board of Appeal has, however, found that the Agency has demonstrated a potential inhalation toxicity concern with regards to pyrogenic SAS (see paragraphs 106 to 130 above).
138. The Board of Appeal will therefore examine below, in Sections II, III and IV, whether the Appellants have identified any other legal flaws that require the first, second and third requests to be annulled in so far as they request additional information on pyrogenic SAS.

II. The Appellants' pleas related to the request for information on physicochemical properties (first request) for pyrogenic SAS only

139. Under the first request the Appellants are required to submit information on seven *'physicochemical properties of each individual SAS form [...] that is manufactured, imported and/or placed on the market'*.
140. In this section, the Board of Appeal will examine the Appellants' arguments regarding the legality of the first request in so far as it is related to pyrogenic SAS only.

The Appellants' plea alleging the violation of the principle of proportionality

Arguments of the Parties

141. The Appellants argue that the Contested Decision is manifestly inappropriate to attain its aim of the protection of human health as there is no legitimate basis for the Agency's purported concern about the toxicity of SAS. The Appellants also argue that the first request is *'especially inapposite to achieve the objective of protecting human health as neither the Agency nor the eMSCA has given any indication of what they intend to do with the massive volume of data that the [request] would generate'*.
142. The Appellants claim that the requested information is not necessary as there are a number of less onerous means that are available to achieve the same objective. For example, the Agency could simply have asked for the maximum and minimum value of each physicochemical characteristic. The Appellants argue that the *'grouping'* they proposed was rejected by the Agency and that this rejection was insufficiently justified and the argumentation for their rejection flawed. The Appellants also argue that the Agency could have asked for fewer characteristics to be tested per form.
143. The Appellants argue that the Contested Decision would impose a burden so severe in terms of testing to be performed and costs as to be disproportionate to any benefits obtained. The Appellants claim that the significant burden on the Appellants must be balanced against, in their opinion, the limited benefits to be gained from this evaluation process. SAS has been on the market and in extremely widespread use for more than a century and there is no evidence that it has adverse effects on human health.
144. The Agency states that, after the adoption of the Contested Decision, the Scientific Committee on Consumer Safety (SCCS) adopted an opinion regarding the use of certain nanomaterial forms of SAS in cosmetic products (SCCS Opinion of 20 March 2015 on Silica, Hydrated Silica, and Silica Surface Modified with Alkyl Silylates (nano form)). The Agency claims that while the SCCS opinion relates primarily to dermal toxicity of forms of SAS, with regard to the need to obtain further information on SAS in general, the SCCS opinion is on the same line as the Contested Decision.

Findings of the Board of Appeal

145. The Board of Appeal notes that the principle of proportionality requires that European Union measures do not exceed the limits of what is appropriate and necessary in order to achieve the objectives legitimately pursued by the measure in question. When there is a choice between several appropriate measures recourse must be had to the least onerous, and the disadvantages caused must not be disproportionate to the aims pursued (judgment of 21 July 2011, *Etimine*, C-15/10, EU:C:2011:504, paragraph 124 and the case-law cited; see also Case A-005-2011, *Honeywell Belgium*, Decision of the Board of Appeal of 29 April 2013, paragraphs 115 to 117, and *International Flavors & Fragrances*, cited in paragraph 53 above, paragraph 72).

146. The Appellants claim that there are hundreds of 'forms' of SAS manufactured, imported or placed on the market by the Appellants. The Agency has not disputed this. The Board of Appeal acknowledges that this figure applies to the 'forms' of SAS currently manufactured and imported by the Appellants and not to pyrogenic SAS, which the Board of Appeal understands is not currently manufactured or imported by either Appellant (see paragraph 5 above). The Board of Appeal also observes that the Contested Decision allows for the possibility of 'grouping' which may reduce the amount of data to be provided by the Appellants. Nonetheless, due to the potential high number of 'forms' of SAS, even if a 'grouping' approach were acceptable to the Agency, the Appellants would still be required to generate a large amount of data on numerous 'forms' of SAS.
147. In the present case, the Board of Appeal has found (see paragraphs 90 to 130 above) that the Agency has demonstrated a potential concern with regards to the inhalation toxicity of pyrogenic SAS only. One of the objectives pursued by the Agency through the Contested Decision is the clarification of the potential concern for the inhalation toxicity of pyrogenic SAS.
148. Through the first request the Agency also seeks to collect information on the physicochemical properties of 'forms' of SAS to help clarify why there are differences in toxicity between the different types and 'forms'. This objective is clearly set out in the Contested Decision which states that:
- 'The available inhalation studies indicate differences in toxicity and potency between different types of SAS, with pyrogenic SAS showing a higher toxic potential than precipitated SAS and silica gel. These differences in potency between SAS types are inextricably bound up with differences in physicochemical characteristics. Physicochemical properties vary significantly between SAS types, but also between different SAS forms within one SAS type [...]. Considering this dependency of toxicity on physicochemical characteristics, identification of the individual forms of SAS for their physicochemical characteristics is required'.*
149. The Board of Appeal finds however that the Agency has not explained in the Contested Decision, or during the present proceedings, how the requested information on the physicochemical properties of 'forms' of SAS would allow the Agency to identify the reasons behind the different toxicity between the different 'forms' and types of SAS. Likewise, the Board of Appeal finds that the Agency has not demonstrated how all the information on the physicochemical 'forms' of pyrogenic SAS will be used to clarify the concern for inhalation toxicity of pyrogenic SAS which, as the Board of Appeal has already found, is the only potential concern demonstrated in the Contested Decision. As a result, the Agency has not demonstrated how the requested information is appropriate to clarify these concerns.
150. The Board of Appeal also considers that the request for a potentially large amount of physicochemical data on all 'forms' of SAS, in order to investigate the difference in toxicity between different 'forms' and types of SAS, is premature. Furthermore, if inhalation toxicity tests on pyrogenic SAS show no concern for inhalation toxicity, or indeed any other toxicity, then all the information submitted on 'forms' could have been in vain. In this respect, once the drivers for toxicity are identified, if they exist at all, then it may be necessary to identify certain physicochemical properties of certain 'forms' and/or types of SAS related to these drivers.

151. The Board of Appeal finds that the cost of generating a potentially large amount of data with no certainty as to how it would be used to clarify the concern, if one is eventually confirmed for pyrogenic SAS, is therefore disproportionate.
152. The Board of Appeal observes that information on physicochemical properties can be relevant to the clarification of the hazards and risks posed by 'forms' and types of SAS. However, such requests for information must be clearly justified by explaining how information on physicochemical and hazardous properties will be used to clarify potential hazards and risks. In this particular case it is not clear whether SAS in any of its types and 'forms' poses a hazard. And if any or all of the 'forms' or types of SAS do pose a hazard, it is not clear what the drivers of that toxicity are. The Board of Appeal accepts that the primary objective of substance evaluation is to clarify such concerns when these concerns are justified but it must be clearly explained how the information requests will do so in a scientifically rigorous as well as, inter alia, proportionate way.
153. In view of the above, the Board of Appeal finds that the Appellants' claim that the first request in so far as it applies to pyrogenic SAS is disproportionate must be upheld. The first request is therefore annulled without it being necessary for the Board of Appeal to examine the Appellants' plea on the alleged breach of Article 25(1) in relation to the that request.

III. The Appellants' pleas in law related to the request for information on sub-chronic toxicity studies (second request) for pyrogenic SAS only

154. By the second request the Appellants are required to provide the following information:
'2. Sub-chronic toxicity study (90-day; OECD 413), in rats via the inhalation route with the following four pyrogenic SAS forms as manufactured that represent:
i. the lowest specific surface area with the lowest number of hydroxyl groups,
ii. the lowest specific surface area with the highest number of hydroxyl groups,
iii. the highest specific surface area with the lowest number of hydroxyl groups,
iv. the highest specific surface area with the highest number of hydroxyl groups [...].'
155. The Board of Appeal notes that the second request is limited to the pyrogenic type of SAS with a request for testing on four 'forms' of pyrogenic SAS.
156. The Board of Appeal will examine below the Appellants' pleas that the second request should be annulled on the grounds of an alleged breach of the principle of proportionality and an alleged breach of Article 25.

A. The alleged breach of the principle of proportionality

Arguments of the Parties

157. The Appellants argue that instead of requiring new toxicological information pursuant to the second request the Agency could have relied on the significant volume of existing data that was available to it. In addition the Agency could, where necessary and appropriate, have requested a re-evaluation of the existing data without requiring additional vertebrate animal testing to be carried out. In particular, it would have been sensible for the Agency to wait for the re-evaluation of the tissue slides used in the Reuzel *et al.* publication which the Appellants had indicated in the Notice of Appeal would be undertaken. At the hearing the Appellants stated that the re-evaluation had taken place and had been submitted in a separate case (Case A-015-2015, *Evonik Degussa*

and Others) against the same Contested Decision. The Appellants claim that the re-evaluation (the PWG review) should also be taken into account in the present appeal.

158. The Appellants, supported by PISC, also argue that rather than requiring the Appellants to carry out 90-day inhalation studies the Agency could have required five-day rather than 90-day studies.

Findings of the Board of Appeal

159. As stated in paragraph 145 above, the principle of proportionality requires that European Union measures do not exceed the limits of what is appropriate and necessary in order to achieve the objectives legitimately pursued by the measure in question. When there is a choice between several appropriate measures recourse must be had to the least onerous, and the disadvantages caused must not be disproportionate to the aims pursued.
160. The objective pursued by the requested testing is to clarify a potential inhalation toxicity concern for pyrogenic SAS from repeated exposure. The Board of Appeal notes that the '*forms*' that need to be tested are clearly defined in relation to surface area and degree of hydroxylation. The Board of Appeal also observes that the requested testing only considers two possible drivers of toxicity, hydroxylation and surface area, when it could potentially have included many more variables in the testing requirements.
161. The Board of Appeal also observes that, as only one commercial product of pyrogenic SAS was tested in the Reuzel *et al.* publication, it is unclear whether the effects identified are relevant to all '*forms*' of pyrogenic SAS. Information on the inhalation toxicity potential of different '*forms*' of pyrogenic SAS is potentially relevant for the purpose of establishing risk management measures. The Board of Appeal also observes that the results of the testing requested should provide information on whether the effects observed in the Reuzel *et al.* publication are reversible and whether the effects are due to particle overload or the toxicity of pyrogenic SAS (see paragraphs 106 to 130 above).
162. The Board of Appeal finds that in the present case it is not appropriate to perform inhalation toxicity testing on only one '*form*' as this will not help the Agency in identifying the potential drivers for toxicity nor will it assist the Agency in clarifying potentially different properties of different '*forms*' of pyrogenic SAS. For this information requirement the Agency has identified two physicochemical properties – number of hydroxyl groups and surface area - as potential drivers for toxicity. The Board of Appeal finds that it is proportionate to require testing that looks at two potential drivers of toxicity.
163. As mentioned in paragraph 119 above, the Appellants were unable to submit the PWG review, which was submitted in Case A-015-2015, *Evonik Degussa and Others*, due to issues related to ownership of that document. Without deciding on whether a document submitted in another, closely related, case should be considered in the present case, the Board of Appeal finds that whilst the PWG review provides further valuable insight into the results of the Reuzel *et al.* publication, it is not capable of clarifying the potential concern identified with regards to pyrogenic SAS. The PWG review is another expert opinion which may come to a different conclusion to that reached by the Agency but does not remove the potential inhalation toxicity concern identified by the Agency. Furthermore, in light of the challenges in re-testing the slides from the 1987 study on which the Reuzel *et al.* publication was based and bearing in mind that the 1987 study was scored as Klimisch 1, there was no reason for the Agency to anticipate that re-examining the results from the Reuzel *et al.* publication would satisfy the objective

pursued. The PWG review also does not answer the questions pertaining to reversibility and whether the observed effects in the Reuzel *et al.* publication are due to particle overload or the toxicity of pyrogenic SAS. The Board of Appeal finds that it is therefore appropriate for the Agency to request sub-chronic inhalation testing on pyrogenic SAS.

164. The Board of Appeal notes that the requirement to test four 'forms' of pyrogenic SAS potentially requires the addressees of the Contested Decision to share information on their commercial products. If the Appellants are concerned about sharing confidential business information, for example on the composition of their products, a third party representative could be appointed to determine the 'forms' that should be tested.
165. The Board of Appeal finds that, in light of the objective legitimately pursued and evidence from the Reuzel *et al.* publication, it is both appropriate and necessary to require a 90-day sub-chronic toxicity study in rats via the inhalation route on four pyrogenic SAS 'forms'. Furthermore, a re-evaluation of existing data and the Reuzel *et al.* publication in particular was not an appropriate measure to clarify fully the potential concern identified. The Appellants' claim that the second request, the sub-chronic toxicity testing on four 'forms' of pyrogenic SAS, is disproportionate must therefore be dismissed.

B. The alleged breach of Article 25(1)

Arguments of the Parties

166. The Appellants claim that neither the Contested Decision itself nor the minutes of the MSC meeting at which it was agreed show that the Agency has paid any or adequate attention to its obligation to assess whether there were suitable alternatives to vertebrate animal testing. Consequently, and independently of the question of whether there were any such alternatives available, the Agency is in breach of Article 25(1) by virtue of its failure to consider the matter properly.
167. In addition, by requiring the Appellants to carry out 90-day studies using four different forms of pyrogenic SAS, the Agency has breached its duty to minimise the harm caused to vertebrate animals.
168. The Appellants also argue that there is a linear relationship between hydroxylation state and specific surface area; that is, high hydroxylation state equates to a high surface area and low hydroxylation state to a low surface area. The second request would therefore require the Appellants to carry out the tests twice on the same 'form'. The Appellants considers that this is clearly unnecessary and is indicative of the Agency's failure to consider its duty to avoid or minimise the harm done by animal testing.
169. The Appellants submit that there were viable alternatives to vertebrate animal testing. In particular, the Agency could have relied on the extensive toxicological information already provided and/or requested re-evaluation of the existing data where appropriate.
170. PISC argues that a short-term (five-day) study could provide equivalent results and therefore by requesting a 90-day study the Agency breached Article 25(1). PISC also argues that the Agency should have conducted a step-wise, or tiered, approach whereby no testing on animals was requested before the physicochemical information on 'forms' requested in the Contested Decision was provided.
171. The Agency argues that the Contested Decision addresses the issue of alternatives to animal testing. As the effects from inhalation exposure were not seen before a 13-week exposure duration, a 28-day repeated dose toxicity study was not an option. Therefore, 'the Agency reflected on possible means to reduce unnecessary testing in the Contested

Decision'. The Agency adds that there is no alternative to testing on vertebrate animals in order to investigate inhalation toxicity from repeated exposure. It can therefore not be decisive whether Article 25 was explicitly referenced or not in the Contested Decision because its objective was met during the decision-making procedure and reflected in the Contested Decision.

Findings of the Board of Appeal

172. At the outset, it should be recalled that Article 13 of the TFEU provides that:
'in formulating and implementing the Union's agriculture, fisheries, transport, internal market [...] policies, the Union and the Member States shall, since animals are sentient beings, pay full regard to the welfare requirements of animals, while respecting the legislative or administrative provisions'.
173. Article 25(1) provides that *'in order to avoid animal testing, testing on vertebrate animals for the purposes of [the REACH] Regulation shall be undertaken only as a last resort'*.
174. The protection of animal welfare is therefore an important consideration in the framework of European Union legislation and the REACH Regulation in particular. The Board of Appeal notes that, under the REACH Regulation, the Agency has a legal obligation to consider animal welfare in its decision-making. Where the Agency requires additional testing pursuant to substance evaluation it must ensure *inter alia* that vertebrate animals are used only as a last resort (Case A-004-2014, *Altair Chimica and Others*, Decision of the Board of Appeal of 9 September 2015, paragraphs 106 to 108).
175. It is in the light of these considerations that the arguments put forward by the Parties and by PISC must be examined.
176. The Board of Appeal notes that the Agency has requested information on four, and potentially only two, *'forms'* of pyrogenic SAS. The Board of Appeal also observes that the information request in the Contested Decision only considers two possible drivers of toxicity, hydroxylation and surface area, when it could potentially have included many more variables in the testing requirements. Consequently, unlike the other requests in the Contested Decision, the Appellants are not required to provide test data on all *'forms'* of SAS nor does the testing address a wide variety of variables requiring the sacrifice of many more vertebrate animals.
177. The Board of Appeal has also found above that there was no requirement for the Agency to wait for the conclusions of the review of the Reuzel *et al.* publication nor to require the conduct of such a review prior to requesting any tests on vertebrate animals (see paragraph 163 above). The Board of Appeal considers that, if the opposite was the case, the delays inherent in having to wait for previous tests on animals to be re-assessed every time a concern is identified, before conducting additional testing, would be incompatible with the primary objective of the REACH Regulation, that is to achieve a high level of protection of human health and the environment.
178. The Board of Appeal also finds that, in light of the pattern of effects shown in the Reuzel *et al.* publication over 13 weeks, a 28-day study would not be of sufficient duration to examine the potential inhalation toxicity concern identified and in particular the effects caused by repeated exposure over a sustained period of time, the reversibility of effects and the relevance and importance of particle overload. The Board of Appeal also notes that there is currently no alternative to testing on vertebrate animals that would allow the assessment of sub-chronic inhalation toxicity.

179. The Board of Appeal also finds that a five-day study, as proposed by PISC, would be insufficient to clarify the objective pursued, the potential inhalation toxicity concern from repeated exposure. A five-day study also could not clarify whether the observed effects in the Reuzel *et al.* publication are reversible and whether they are due to particle overload or the toxicity of pyrogenic SAS.
180. The Appellants also argue that the Contested Decision breaches Article 25 as it allegedly requests the Appellants to perform the study on the same 'form' of pyrogenic SAS twice due to the linear correlation between surface area and the number of hydroxyl groups.
181. This issue of the 'forms' to be tested was discussed between the eMSCA and the registrants of SAS and was addressed in the Contested Decision and in the submissions in this appeal. According to the Contested Decision:
- 'To address the concern, information on the most potent forms of SAS is required. Therefore, additional inhalation information on the four indicated forms is requested to ensure that the most potent forms are studied. It cannot be ruled out that another form of SAS than the ones currently tested may be more potent and induce fibrosis at a lower concentration, resulting in a lower DNEL. Therefore, it is highly relevant to perform the requested 90-day toxicity study with the requested forms'.*
182. In the same vein the minutes of the 39th Meeting of the MSC on 8-11 December 2014 state that:
- 'The proposed decision contains requests to test on only four of these forms, i.e. testing on the most relevant forms. The eMSCA expressed concern that the differences in surface area clearly indicated by the Registrants could lead to differences in toxicity hence they are requesting for a 90-day inhalation study on four SAS forms'.*
183. The Board of Appeal observes that there is a disagreement on the link between surface area and number of hydroxyl groups, whether there is a linear correlation between the two, and whether this correlation covers the full range of surface areas and hydroxylation states for the registered 'forms' of SAS. The Board of Appeal, in the absence of detailed information on the 'forms' to be tested, as identified in the Contested Decision, cannot say which Party is correct in this regard. However, the Board of Appeal observes that if, in practice, the four different 'forms' identified in the Contested Decision only result in two different samples for testing purposes then only the two samples should be tested. If this is the case, the Appellants should provide a clear justification to this effect in the registration dossier update. The Board of Appeal therefore considers that the Agency has not breached Article 25 in this respect.
184. The Board of Appeal also finds that the Appellants' argument that the Contested Decision makes no reference to the consideration of alternatives to animal testing is incorrect. The Contested Decision states in this regard that:
- 'As an alternative, in case for one of the identified forms a sub-chronic toxicity study (90-day, via inhalation) is available (taking into account the modifications to OECD 413 indicated above), and the tested form [...] is fully characterised according to [first request] of [the Contested Decision], this information may be provided to cover the information request for this one form'.*
185. The Appellants' claim that the Agency breached Article 25 is therefore dismissed.
186. The Appellants' pleas in relation to the second request are therefore dismissed in their entirety.

IV. The Appellants' pleas related to the uses of pyrogenic SAS only (third request)

187. By way of the third request the Appellants are required to provide '*[i]nformation on the uses of each individual form of SAS [...] that is manufactured, imported and/or placed on the market.*' As the Board of Appeal has already annulled the third request insofar as it applies to precipitated SAS, silica gel and colloidal SAS, the Board of Appeal will examine this plea with regards to the uses of pyrogenic SAS only.
188. In support of their claim that the third request should be annulled, the Appellants claim first that the request breaches the principle of proportionality and second that the Agency lacks the competence to request such data on uses.

Alleged breach of the principle of proportionality

Arguments of the Parties

189. The Appellants claim that, as manufacturers and importers of SAS rather than users, they '*would have to seek information from downstream users on the thousands of uses of the various forms of SAS*'. The Appellants also claim that this would be an extremely time-consuming and fruitless exercise, which in any event might also raise concerns under European Union competition law. The Appellants claim that the third request could have been made to the downstream users of SAS.
190. The Appellants argue that if information on uses is necessary to permit the timely adoption of risk management measures, then the Agency should pursue a targeted request for relevant data if the existence of an actual risk is established; and even then only in relation to the '*form*' or '*forms*' of SAS demonstrated to pose a risk.
191. The Agency states that the request for toxicological information aims at confirming whether there is a difference between types and corresponding '*forms*' of SAS. Risk management measures taking into account the difference in toxicity of types of SAS and corresponding '*forms*' may have to be adopted in a timely manner. However, such measures would only be proportionate if the actual uses per type and '*form*' are known to the authorities, so that the measure can take account of the actual exposure to various types and '*forms*' of the substance. The requested information on uses is therefore necessary.
192. The Contested Decision states that '*in the registration dossier, a list of uses of SAS by industrial workers, professional workers and consumer is included*'. However, the uses are described without distinguishing between the type and '*form*' of SAS.
193. The Agency states that waiting for the toxicity profile of the types and '*forms*' of SAS to be determined before requesting information on uses would imply that a second, or even third round of substance evaluation decision-making would become necessary. Given that the information on uses should already be readily available the request only requires a clarification as to which type or '*form*' correspond to the uses identified.

Findings of the Board of Appeal

194. As an initial observation, the Board of Appeal notes that the Appellants have stated that whilst they do not manufacture or import pyrogenic SAS they did intend to register it (see paragraph 5 above). As the Appellants have stated that they may manufacture or import pyrogenic SAS in the future and taking into account the fact that the Contested Decision does not specify who has to submit information on uses, it is necessary to consider the Appellants' plea with regard to the proportionality of the third request.

195. As stated in paragraph 145, the principle of proportionality requires that European Union measures do not exceed the limits of what is appropriate and necessary in order to achieve the objectives legitimately pursued by the measure in question. When there is a choice between several appropriate measures recourse must be had to the least onerous, and the disadvantages caused must not be disproportionate to the aims pursued.
196. The Board of Appeal finds that, in the absence of information about the inhalation toxicity of pyrogenic SAS, the request for further information on uses is premature. Furthermore, whilst information on uses may be relevant for the introduction of appropriate risk management measures, without some understanding of the drivers of toxicity, if any, it is not possible to identify which characteristics may be relevant for the identification of '*forms*' and the uses thereof for risk management purposes. The Agency has not therefore demonstrated why, at this stage, the information on uses is necessary.
197. In the interests of clarity, the Board of Appeal recognises that information on uses may be relevant information to request pursuant to a substance evaluation. However, it must be clear how information on uses will be used to clarify the concern, particularly with regards to improved risk management measures.
198. The Appellants' plea that the third request breaches the principle of proportionality is upheld and there is therefore no need to examine the Appellants' plea regarding the Agency's competence to request data on uses.
199. In view of the above, the Board of Appeal finds that the third request, having already been annulled in so far as it relates to the non-pyrogenic types of SAS, must also be annulled with regard to pyrogenic SAS and therefore in its entirety.

Refund of the appeal fee

200. In accordance with Article 10(4) of Commission Regulation (EC) No 340/2008 on the fees and charges payable to the European Chemicals Agency pursuant to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) (OJ L 107, 17.4.2008, p. 6), the appeal fee shall be refunded if the appeal is decided in favour of an appellant.
201. In the present case, four of the five information requirements set out in the Contested Decision have been annulled. The Board of Appeal finds in the circumstances of the current case that the appeal must be considered as having been decided in favour of the Appellants.
202. The appeal fee shall therefore be refunded.

Effects of the Contested Decision

203. According to Article 91(2), an appeal has suspensive effect.
204. The Contested Decision, which is partially annulled in the present appeal proceedings, required the registrants, now the Appellants, to submit the required information by 20 March 2017, which is two years and nine days from the date of adoption of the Contested Decision. The Board of Appeal considers however that, because of the duration of the present appeal proceedings, the deadline set in the Contested Decision should be interpreted, in the light of the principle of suspensive effect laid down in Article 91(2), as if it referred to two years and nine days from the date of notification of the final decision of the Board of Appeal.

205. Consequently, the information required by the part of the Contested Decision which is not annulled, namely a sub-chronic toxicity study (90-day; OECD 413), in rats via the inhalation route with four pyrogenic SAS '*forms*' (Section II, point 2 of the Contested Decision), shall be submitted within two years and nine days from the date of notification of this Decision of the Board of Appeal.

On those grounds,

THE BOARD OF APPEAL

hereby:

- 1. Annuls the Agency's Decision of 11 March 2015 on the substance evaluation of silicon dioxide in so far as it requests:**
 - **information on seven physicochemical properties of each individual SAS '*form*' that is manufactured, imported and/or placed on the market (the first request),**
 - **information on the uses of each individual '*form*' of SAS that is manufactured, imported and/or placed on the market (the third request),**
 - **information on eight physicochemical properties of each individual surface-treated SAS '*form*' that is manufactured, imported and/or placed on the market (the fourth request), and**
 - **all toxicological information on surface-treated SAS as manufactured, imported and/or placed on the market as available to the Registrant(s) of SAS (the fifth request).**
- 2. Dismisses the appeal as regards the request for information on a sub-chronic toxicity study (90-day; OECD 413), in rats via the inhalation route with four pyrogenic SAS '*forms*' (the second request). This information shall be provided by 9 July 2019.**
- 3. Decides that the appeal fee shall be refunded.**

Mercedes ORTUÑO
Chairman of the Board of Appeal

Marc GOODACRE
On behalf of the Registrar of the Board of Appeal