Quality Assessment Tool tables of included studies

Dallaire R, Muckle G, Dewailly E, Jacobson SW, Jacobson JL, Sandanger TM, Sandau CD, Ayotte P. (2009). Thyroid hormone levels of pregnant inuit women and their infants exposed to environmental contaminants. Environ Health Perspect, 117(6), 1014-1020.					Requires Yes or NA for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described	Yes	No	Can´t tell	NA	x

Dallaire R, Muckle G, Dewailly E, Jacobson SW, Jacobson JL, Sandanger TM, Sandau CD, Ayotte P. (2009). Thyroid hormone levels of pregnant inuit women and their infants exposed to environmental contaminants. Environ Health Perspect, 117(6), 1014-1020.					Requires Yes or NA for level A B C
and taken into consideration?					
7. Statistical power (key studies)					
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
9. Summary of the study quality	B				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Forns J, Torrent M, Garcia-Esteban R, Grellier J, Gascon M, Julvez J, Guxens M, Grimalt JO, Sunyer J. (2012). Prenatal exposure to polychlorinated biphenyls and child neuropsychological development in 4-year-olds: an analysis per congener and specific cognitive domain. Sci Total Environ, 432, 338-343.					Requires Yes or NA for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x

Forns J, Torrent M, Garcia-Esteban R, Grellier J, Gascon M, Julvez J, Guxens M, Grimalt JO, Sunyer J. (2012). Prenatal exposure to polychlorinated biphenyls and child neuropsychological development in 4-year-olds: an analysis per congener and specific cognitive domain. Sci Total Environ, 432, 338-343.					Requires Yes or NA for level A B C
7. Statistical power (key studies)					
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
9. Summary of the study quality	B				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Gascon M, Verner MA, Guxens M, Grimalt JO, Forns J, Ibarluzea J, Lertxundi N, Ballester F, Llop S, Haddad S, Sunyer J, Vrijheid M. (2013). Evaluating the neurotoxic effects of lactational exposure to persistent organic pollutants (POPs) in Spanish children. Neurotoxicology, 34, 9-15.					Requires Yes or NA for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x

Gascon M, Verner MA, Guxens M, Grimalt JO, Forns J, Ibarluzea J, Lertxundi N, Ballester F, Llop S, Haddad S, Sunyer J, Vrijheid M. (2013). Evaluating the neurotoxic effects of lactational exposure to persistent organic pollutants (POPs) in Spanish children. Neurotoxicology, 34, 9-15.					Requires Yes or NA for level A B C
7. Statistical power (key studies)					
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
9. Summary of the study quality	B+				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Gladen BC, Ragan NB, Rogan WJ. (2000). Pubertal growth and development and prenatal and lactational exposure to polychlorinated biphenyls and dichlorodiphenyl dichloroethene. J Pediatr, 136(4), 490-496.		Requires Yes for level A B C
1. General questions and study design		
a) Research question clearly formulated?	Yes No Can´t tell NA	x x
b) Endpoint/outcome clearly defined?	Yes No Can´t tell NA	x x
c) Was the study design suited to test the research hypothesis?	Yes No Can´t tell NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*		
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes No Can´t tell NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes No Can´t tell NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes No Can´t tell NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes No Can´t tell NA	x x
3. Breastmilk consumption/contaminant exposure		
a) Type of contaminant exposure reported in sufficient detail?	Yes No Can´t tell NA	x x
b) Is length of breastfeeding clearly defined?	Yes No Can´t tell NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes No Can´t tell NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes No Can´t tell NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes No Can´t tell NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes No Can´t tell NA	x x
4. Relevance for the present purpose	Yes No Requires Yes for further questions below	
5. Gestational length		
a) Are premature infants separated in statistical analysis?	Yes No Can´t tell NA	x
6. Confounding (pairity, mothers age etc.)		
a) Were important confounders identified/ascertained and considered by authors?	Yes (although maternal height not in growth model)	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes No Can´t tell NA	x

Gladen BC, Ragan NB, Rogan WJ. (2000). Pubertal growth and development and prenatal and lactational exposure to polychlorinated biphenyls and dichlorodiphenyl dichloroethene. J Pediatr, 136(4), 490-496.					Requires Yes for level A B C
7. Statistical power (key studies)					
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis ppropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
e) Ascertainment/detection bias considered (eg. cases detected due to screening)?	Yes	No	Can´t tell	NA	x
9. Summary of the study quality	B				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Gladen BC, Rogan WJ. (1991). Effects of perinatal polychlorinated biphenyls and dichlorodiphenyl dichloroethene on later development. J Pediatr, 119(1 Pt 1), 58-63.					Requires Yes for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x
7. Statistical power (key studies)					

Gladen BC, Rogan WJ. (1991). Effects of perinatal polychlorinated biphenyls and dichlorodiphenyl dichloroethene on later development. J Pediatr, 119(1 Pt 1), 58-63.					Requires Yes for level A B C
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis ppropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
e) Ascertainment/detection bias considered (eg. cases detected due to screening)?	Yes	No	Can´t tell	NA	x
9. Summary of the study quality	B				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Grandjean P, Budtz-Jorgensen E, Steuerwald U, Heinzow B, Needham LL, Jorgensen PJ, Weihe P. (2003). Attenuated growth of breast-fed children exposed to increased concentrations of methylmercury and polychlorinated biphenyls. FASEB J, 17(6), 699-701.					Requires Yes or NA for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x
7. Statistical power (key studies)					

Grandjean P, Budtz-Jorgensen E, Steuerwald U, Heinzow B, Needham LL, Jorgensen PJ, Weihe P. (2003). Attenuated growth of breast-fed children exposed to increased concentrations of methylmercury and polychlorinated biphenyls. FASEB J, 17(6), 699-701.					Requires Yes or NA for level A B C
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
9. Summary of the study quality	B				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Grandjean P, Poulsen LK, Heilmann C, Steuerwald U, Weihe P. (2010). Allergy and sensitization during childhood associated with prenatal and lactational exposure to marine pollutants. Environ Health Perspect, 118(10), 1429-1433.					Requires Yes or NA for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x
7. Statistical power (key studies)					

Grandjean P, Poulsen LK, Heilmann C, Steuerwald U, Weihe P. (2010). Allergy and sensitization during childhood associated with prenatal and lactational exposure to marine pollutants. Environ Health Perspect, 118(10), 1429-1433.					Requires Yes or NA for level A B C
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
9. Summary of the study quality	B				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Grandjean P, Weihe P, White RF. (1995). Milestone development in infants exposed to methylmercury from human milk. Neurotoxicology, 16(1), 27-33.					Requires Yes for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x
7. Statistical power (key studies)					

Grandjean P, Weihe P, White RF. (1995). Milestone development in infants exposed to methylmercury from human milk. Neurotoxicology, 16(1), 27-33.					Requires Yes for level A B C
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
e) Ascertainment/detection bias considered (eg. cases detected due to screening)?	Yes	No	Can´t tell	NA	x
9. Summary of the study quality	B				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Heilmann C, Budtz-Jorgensen E, Nielsen F, Heinzow B, Weihe P, Grandjean P. (2010). Serum concentrations of antibodies against vaccine toxoids in children exposed perinatally to immunotoxicants. Environ Health Perspect, 118(10), 1434-1438.					Requires Yes or NA for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x
7. Statistical power (key studies)					

Heilmann C, Budtz-Jorgensen E, Nielsen F, Heinzow B, Weihe P, Grandjean P. (2010). Serum concentrations of antibodies against vaccine toxoids in children exposed perinatally to immunotoxicants. Environ Health Perspect, 118(10), 1434-1438.					Requires Yes or NA for level A B C
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
9. Summary of the study quality	B				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Huisman M, Koopman-Esseboom C, Lanting CI, van der Paauw CG, Tuinstra LG, Fidler V, Weisglas-Kuperus N, Sauer PJ, Boersma ER, Touwen BC. (1995). Neurological condition in 18-month-old children perinatally exposed to polychlorinated biphenyls and dioxins. Early Hum Dev, 43(2), 165-176.					Requires Yes or NA for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x

Huisman M, Koopman-Esseboom C, Lanting CI, van der Paauw CG, Tuinstra LG, Fidler V, Weisglas-Kuperus N, Sauer PJ, Boersma ER, Touwen BC. (1995). Neurological condition in 18-month-old children perinatally exposed to polychlorinated biphenyls and dioxins. Early Hum Dev, 43(2), 165-176.					Requires Yes or NA for level A B C
7. Statistical power (key studies)					
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
9. Summary of the study quality	B				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Jacobson JL, Jacobson SW, Humphrey HE. (1990). Effects of exposure to PCBs and related compounds on growth and activity in children. Neurotoxicol Teratol, 12(4), 319-326.					Requires Yes or NA for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x
7. Statistical power (key studies)					

Jacobson JL, Jacobson SW, Humphrey HE. (1990). Effects of exposure to PCBs and related compounds on growth and activity in children. Neurotoxicol Teratol, 12(4), 319-326.					Requires Yes or NA for level A B C
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis ppropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
9. Summary of the study quality	B				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Jensen TK, Grandjean P, Jorgensen EB, White RF, Debes F, Weihe P. (2005). Effects of breast feeding on neuropsychological development in a community with methylmercury exposure from seafood. J Expo Anal Environ Epidemiol, 15(5), 423-430.					Requires Yes for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x
7. Statistical power (key studies)					

Jensen TK, Grandjean P, Jorgensen EB, White RF, Debes F, Weihe P. (2005). Effects of breast feeding on neuropsychological development in a community with methylmercury exposure from seafood. J Expo Anal Environ Epidemiol, 15(5), 423-430.					Requires Yes for level A B C
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
e) Ascertainment/detection bias considered (e.g. cases detected due to screening)?	Yes	No	Can´t tell	NA	x
9. Summary of the study quality	B				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Jusko TA, Sonneborn D, Palkovicova L, Kocan A, Drobna B, Trnovec T, Hertz-Picciotto I. (2012). Pre- and postnatal polychlorinated biphenyl concentration and longitudinal measures of thymus volume in infants. Environ Health Perspect, 120(4), 595-600.					Requires Yes for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and	Yes	No	Can´t tell	NA	x x

Jusko TA, Sonneborn D, Palkovicova L, Kocan A, Drobna B, Trnovec T, Hertz-Picciotto I. (2012). Pre- and postnatal polychlorinated biphenyl concentration and longitudinal measures of thymus volume in infants. Environ Health Perspect, 120(4), 595-600.		Requires Yes for level A B C
considered by authors?		
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes No Can´t tell NA	x
7. Statistical power (key studies)		
a) Was the study power considered and sample size and power calculations reported?	Yes No Can´t tell NA	x
b) In view of multiple tests, were by chance findings considered?	Yes No Can´t tell NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes No Can´t tell NA	x
8. Statistical analysis		
a) Follow-up period clearly identified?	Yes No Can´t tell NA	x
b) Loss to follow up described?	Yes No Can´t tell NA	x
c) Statistical analysis appropriately handled?	Yes No Can´t tell NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes No Can´t tell NA	x x
9. Summary of the study quality	B	

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Koopman-Esseboom C, Weisglas-Kuperus N, de Ridder MA, van der Paauw CG, Tuinstra LG, Sauer PJ. (1996). Effects of polychlorinated biphenyl/dioxin exposure and feeding type on infants' mental and psychomotor development. Pediatrics, 97(5), 700-706.					Requires Yes or NA for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x

Koopman-Esseboom C, Weisglas-Kuperus N, de Ridder MA, van der Paauw CG, Tuinstra LG, Sauer PJ. (1996). Effects of polychlorinated biphenyl/dioxin exposure and feeding type on infants' mental and psychomotor development. Pediatrics, 97(5), 700-706.					Requires Yes or NA for level A B C
7. Statistical power (key studies)					
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
9. Summary of the study quality	B+				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Lanting CI, Patandin S, Fidler V, Weisglas-Kuperus N, Sauer PJ, Boersma ER, Touwen BC. (1998). Neurological condition in 42-month-old children in relation to pre- and postnatal exposure to polychlorinated biphenyls and dioxins. Early Hum Dev, 50(3), 283-292.					Requires Yes or NA for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x

Lanting CI, Patandin S, Fidler V, Weisglas-Kuperus N, Sauer PJ, Boersma ER, Touwen BC. (1998). Neurological condition in 42-month-old children in relation to pre- and postnatal exposure to polychlorinated biphenyls and dioxins. Early Hum Dev, 50(3), 283-292.					Requires Yes or NA for level A B C
7. Statistical power (key studies)					
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
9. Summary of the study quality	B+				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Patandin S, Lanting CI, Mulder PG, Boersma ER, Sauer PJ, Weisglas-Kuperus N. (1999). Effects of environmental exposure to polychlorinated biphenyls and dioxins on cognitive abilities in Dutch children at 42 months of age. J Pediatr, 134(1), 33-41					Requires Yes or NA for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x
7. Statistical power (key studies)					

Patandin S, Lanting CI, Mulder PG, Boersma ER, Sauer PJ, Weisglas-Kuperus N. (1999). Effects of environmental exposure to polychlorinated biphenyls and dioxins on cognitive abilities in Dutch children at 42 months of age. J Pediatr, 134(1), 33-41					Requires Yes or NA for level A B C
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
9. Summary of the study quality	B+				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Rogan WJ, Gladen BC. (1991). PCBs, DDE, and child development at 18 and 24 months. Ann Epidemiol, 1(5), 407-413.					Requires Yes or NA for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x
7. Statistical power (key studies)					

Rogan WJ, Gladen BC. (1991). PCBs, DDE, and child development at 18 and 24 months. Ann Epidemiol, 1(5), 407-413.					Requires Yes or NA for level A B C
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
9. Summary of the study quality	B				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Sunyer J, Torrent M, Garcia-Esteban R, Ribas-Fito N, Carrizo D, Romieu I, Anto JM, Grimalt JO. (2006). Early exposure to dichlorodiphenyldichloroethylene, breastfeeding and asthma at age six. Clin Exp Allergy, 36(10), 1236-1241.					Requires Yes for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes				
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x
7. Statistical power (key studies)					

Sunyer J, Torrent M, Garcia-Esteban R, Ribas-Fito N, Carrizo D, Romieu I, Anto JM, Grimalt JO. (2006). Early exposure to dichlorodiphenyldichloroethylene, breastfeeding and asthma at age six. Clin Exp Allergy, 36(10), 1236-1241.					Requires Yes for level A B C
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis ppropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
e) Ascertainment/detection bias considered (eg. cases detected due to screening)?	Yes	No	Can´t tell	NA	x
9. Summary of the study quality	B				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Verner MA, Plusquellec P, Muckle G, Ayotte P, Dewailly E, Jacobson SW, Jacobson JL, Charbonneau M, Haddad S. (2010). Alteration of infant attention and activity by polychlorinated biphenyls: unravelling critical windows of susceptibility using physiologically based pharmacokinetic modeling. Neurotoxicology, 31(5), 424-431.					Requires Yes or NA for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x

Verner MA, Plusquellec P, Muckle G, Ayotte P, Dewailly E, Jacobson SW, Jacobson JL, Charbonneau M, Haddad S. (2010). Alteration of infant attention and activity by polychlorinated biphenyls: unravelling critical windows of susceptibility using physiologically based pharmacokinetic modeling. Neurotoxicology, 31(5), 424-431.					Requires Yes or NA for level A B C
7. Statistical power (key studies)					
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
9. Summary of the study quality	B				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Vreugdenhil HJ, Slijper FM, Mulder PG, Weisglas-Kuperus N. (2002). Effects of perinatal exposure to PCBs and dioxins on play behavior in Dutch children at school age. Environ Health Perspect, 110(10), A593-A598.					Requires Yes or NA for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x
7. Statistical power (key studies)					

Vreugdenhil HJ, Slijper FM, Mulder PG, Weisglas-Kuperus N. (2002). Effects of perinatal exposure to PCBs and dioxins on play behavior in Dutch children at school age. Environ Health Perspect, 110(10), A593-A598.					Requires Yes or NA for level A B C
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
9. Summary of the study quality	B+				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Vreugdenhil HJ, Lanting CI, Mulder PG, Boersma ER, Weisglas-Kuperus N. (2002). Effects of prenatal PCB and dioxin background exposure on cognitive and motor abilities in Dutch children at school age. J Pediatr, 140(1), 48-56.					Requires Yes or NA for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x
7. Statistical power (key studies)					

Vreugdenhil HJ, Lanting CI, Mulder PG, Boersma ER, Weisglas-Kuperus N. (2002). Effects of prenatal PCB and dioxin background exposure on cognitive and motor abilities in Dutch children at school age. J Pediatr, 140(1), 48-56.					Requires Yes or NA for level A B C
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
9. Summary of the study quality	B+				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Walkowiak J, Wiener JA, Fastabend A, Heinzow B, Kramer U, Schmidt E, Steingruber HJ, Wundram S, Winneke G. (2001). Environmental exposure to polychlorinated biphenyls and quality of the home environment: effects on psychodevelopment in early childhood. Lancet, 358(9293), 1602-1607.					Requires Yes or NA for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x

Walkowiak J, Wiener JA, Fastabend A, Heinzow B, Kramer U, Schmidt E, Steingruber HJ, Wundram S, Winneke G. (2001). Environmental exposure to polychlorinated biphenyls and quality of the home environment: effects on psychodevelopment in early childhood. Lancet, 358(9293), 1602-1607.					Requires Yes or NA for level A B C
7. Statistical power (key studies)					
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
9. Summary of the study quality	B				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Weisglas-Kuperus N, Patandin S, Berbers GA, Sas TC, Mulder PG, Sauer PJ, Hooijkaas H. (2000). Immunologic effects of background exposure to polychlorinated biphenyls and dioxins in Dutch preschool children. Environ Health Perspect, 108(12), 1203-1207.					Requires Yes or NA for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x

Weisglas-Kuperus N, Patandin S, Berbers GA, Sas TC, Mulder PG, Sauer PJ, Hooijkaas H. (2000). Immunologic effects of background exposure to polychlorinated biphenyls and dioxins in Dutch preschool children. Environ Health Perspect, 108(12), 1203-1207.					Requires Yes or NA for level A B C
7. Statistical power (key studies)					
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
9. Summary of the study quality	B+				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.

Winneke G, Kramer U, Sucker K, Walkowiak J, Fastabend A, Heinzow B, Steingruber HJ. (2005). PCB-related neurodevelopmental deficit may be transient: follow-up of a cohort at 6 years of age. Environ Toxicol Pharmacol, 19(3), 701-706.					Requires Yes or NA for level A B C
1. General questions and study design					
a) Research question clearly formulated?	Yes	No	Can´t tell	NA	x x
b) Endpoint/outcome clearly defined?	Yes	No	Can´t tell	NA	x x
c) Was the study design suited to test the research hypothesis?	Yes	No	Can´t tell	NA	x x
2. Sampling (*Ascertainment of cases and non-cases)*					
a) Source population/study base well defined? Recruitment done in an acceptable way?	Yes	No	Can´t tell	NA	x x
b) Criteria for inclusion/exclusion clearly formulated and sufficient?	Yes	No	Can´t tell	NA	x x
c) Time points of data collection clearly described (year of sampling, month or year of follow-up, child's age etc.)	Yes	No	Can´t tell	NA	x
d) Health outcome/endpoint clearly ascertained and assessed?	Yes	No	Can´t tell	NA	x x
3. Breastmilk consumption/contaminant exposure					
a) Type of contaminant exposure reported in sufficient detail?	Yes	No	Can´t tell	NA	x x
b) Is length of breastfeeding clearly defined?	Yes	No	Can´t tell	NA	x x
c) Is it clearly defined whether the infants have been fully breastfed (=exclusive+predominantly) or partly breastfed (all other breastfeeding)?	Yes	No	Can´t tell	NA	x
d) Time period between contaminant assessment and diagnosis acceptable?	Yes	No	Can´t tell	NA	x if relevant
e) Is prenatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
f) Is postnatal **contaminant** exposure assessed appropriately?	Yes	No	Can´t tell	NA	x x
4. Relevance for the present purpose	Yes	No	Requires Yes for further questions below		
5. Gestational length					
a) Are premature infants separated in statistical analysis?	Yes	No	Can´t tell	NA	x
6. Confounding (pairity, mothers age etc.)					
a) Were important confounders identified/ascertained and considered by authors?	Yes	No	Can´t tell	NA	x x
b) The distribution of confounders similar in cases and non-cases adequately described and taken into consideration?	Yes	No	Can´t tell	NA	x
7. Statistical power (key studies)					

Winneke G, Kramer U, Sucker K, Walkowiak J, Fastabend A, Heinzow B, Steingruber HJ. (2005). PCB-related neurodevelopmental deficit may be transient: follow-up of a cohort at 6 years of age. Environ Toxicol Pharmacol, 19(3), 701-706.					Requires Yes or NA for level A B C
a) Was the study power considered and sample size and power calculations reported?	Yes	No	Can´t tell	NA	x
b) In view of multiple tests, were by chance findings considered?	Yes	No	Can´t tell	NA	x
c) Sufficient size of study population and no. of outcomes/cases?	Yes	No	Can´t tell	NA	x
8. Statistical analysis					
a) Follow-up period clearly identified?	Yes	No	Can´t tell	NA	x
b) Loss to follow up described?	Yes	No	Can´t tell	NA	x
c) Statistical analysis appropriately handled?	Yes	No	Can´t tell	NA	x
d) Relevant confounders adequately handled: Restriction, Stratified analysis, Multivariate modelling, Interaction tested?	Yes	No	Can´t tell	NA	x x
9. Summary of the study quality	B				

A The results from studies that have an acceptably low level of bias are considered valid. These studies adhere mostly to the commonly held concepts of high quality including the following: a comprehensive study design; clear description of the participants, setting, interventions, and control group(s); appropriate measurement of outcomes; appropriate statistical and analytical methods and reporting; no reporting errors; less than 30% percent dropout (depending on the length of the study see the QAT for clinical studies) or over 50% participation rate for prospective cohort studies; clear reporting of dropouts; and no obvious bias. Where appropriate, studies must provide a valid estimation of contaminant exposure, from assessments and/or biomarkers with a reasonable range of measurement error, and justification for approaches to control for confounding in the design and analyses.

B Studies may have some bias, but not sufficient to invalidate the results. They do not meet all the criteria in category "A". They have some deficiencies but none likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

C Studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; there are large amounts of missing information, or discrepancies in reporting.