

**Appendix A**  
**The Appraisal Standard of Newcastle/Ottawa Scale**

**Selection**

- 1) Representativeness of the exposed group/cohort
  - a) Truly representative of the average farmers or pesticides applicators in the community\*
  - b) Somewhat representative of the average farmers or pesticides applicators in the community\*
  - c) Selected group of users (e.g. factory workers, volunteers)
  - d) No description of the derivation of the group
  
- 2) Selection of the non-exposed group/cohort
  - a) Drawn from the same community as the exposed group\*
  - b) Drawn from a different source
  - c) No description of the derivation of the non-exposed group
  
- 3) Ascertainment of exposure
  - a) Secure record (e.g. biomarkers)\*
  - b) Structured interview or questionnaire\*
  - c) Written self reports
  - d) No description
  
- 4) Demonstration that outcome of interest was not present at start of study (*Cohort Studies Only*)
  - a) Yes\*
  - b) No

**Confounder**

- 1) Comparability of groups on the basis of the design or analysis
  - a) Study controls for age and education\*
  - b) Study controls for any additional factor\* (e.g. alcohol consumption, smoking, and first language)

**Outcome**

- 1) Assessment of outcome
  - a) Independent blind assessment\*
  - b) Record linkage\*
  - c) Self reports

- d) No description
- 2) Was follow-up long enough for outcomes to occur (*Cohort Studies Only*)
    - a) Yes (select an adequate follow up period for outcome of interest)\*
    - b) No
  - 3) Adequacy of follow up of cohorts (*Cohort Studies Only*)
    - a) Complete follow up – all subjects accounted for\*
    - b) Subjects lost to follow up unlikely to introduce bias – small number lost - > 70% follow up, or description provided of those lost\*
    - c) Follow up < 70% and no description of those lost
    - d) No statement

*Case Control Studies:*

**Selection**

- 1) Is the case definition adequate?
  - a) Yes, with independent validation\*
  - b) Yes, e.g. record linkage on self reports
  - c) No description
- 2) Representativeness of the cases
  - a) Consecutive or obviously representative series of cases\*
  - b) Potential for selection biases or non stated
- 3) Selection of Controls
  - a) Community controls\*
  - b) Hospital controls
  - c) No description
- 4) Definition of Controls
  - a) No history of disease (endpoint)\*
  - b) No description of source

**Confounder**

- 1) Comparability of cases and controls on the basis of design or analysis
  - a) Study controls for age and education\*
  - b) Study controls for any additional factor\*

## **Exposure**

- 1) Ascertainment of exposure
    - a) Secure record (e.g. biomarkers)\*
    - b) Structured interview where blind to case/control status\*
    - c) Interview not blinded to case/ control status
    - d) Written self reports or medical record only
    - e) No description
  
  - 2) Same method of ascertainment for cases and controls
    - a) Yes\*
    - b) No
  
  - 3) Non-Response rate
    - a) Same rate for both groups\*
    - b) Non respondents described
    - c) Rate different and no designation
- \*: plus one point

There are five items in cross-sectional studies and eight items in cohort and case control studies, respectively. The quality of the studies was defined as follows.

### *Cross-sectional Studies:*

Very Good Studies: 5 points

Good Studies: 4 points

Satisfactory Studies: 3 points

Unsatisfactory Studies: 0 to 2 points

### *Cohort / Case control Studies:*

Very Good Studies: 7 to 8 points

Good Studies: 5 to 6 points

Satisfactory: 4 points

Unsatisfactory Studies: 0 to 3 points

## Appendix B

**Table1 Quality Appraisal (Cross-sectional Studies)**

	Cole et al 1997	Dassanaya ke et al 2009	Farahat et al 2003	Fiedler et al 1997	Korsak et al 1977	Levin et al 1976
<b>Selection</b>						
1) Representativeness of the exposed group						
a) Truly representative of the average farmers or pesticides applicators in the community						
b) Somewhat representative of the average or pesticides applicators in the community	a) (+1)	b) (+1)	c) (0)	a) (+1)	b) (+1)	b) (+1)
c) Selected group of users						
d) No description of the derivation of the group						
2) Selection of the non exposed group						
a) Drawn from the same community as the exposed group						
b) Drawn from a different source	a) (+1)	b) (0)	b) (0)	a) (+1)	a) (+1)	b) (0)
c) No description of the derivation of the non exposed group						
3) Ascertainment of exposure						
a) Secured record (e.g. biomarkers)						
b) Structured interview or questionnaire	b) (+1)	d) (0)	a) (+1)	b) (+1)	a) (+1)	a) (+1)
c) Written self report						
d) No description						
<b>Confounders</b>						
1) Comparability of groups on the basis of the design or analysis	b) (+1)	- (0)	a) (+1)	- (0)	- (0)	- (0)
a) Study controls for age and						

education						
b) Study controls for any additional factor (e.g. alcohol consumption, smoking, and first language)						
<b>Outcome</b>						
1) Assessment of outcome						
a) Independent blind assessment	a) (+1)	b) (+1)	d) (0)	b) (+1)	d) (0)	a) (+1)
b) Record linkage						
c) Self report						
d) No description						
Overall Score	5/5 Very Good	2/5 Unsatisfactory	2/5 Unsatisfactory	4/5 Good	3/5 Satisfactory	3/5 Satisfactory

Continued...

Table1 Continued

	London et al 1997	London et al 1998	Maizish et al 1987	Rodnitzky et l 1975	Roldan-Tapia et al 2005
<b>Selection</b>					
1) Representativeness of the exposed group					
a) Truly representative of the average farmers or pesticides applicators in the community					
b) Somewhat representative of the average or pesticides applicators in the community	b) (+1)	a) (+1)	c) (0)	c) (0)	a) (+1)
c) Selected group of users					
d) No description of the derivation of the group					
2) Selection of the non exposed group					
a) Drawn from the same community as the exposed group	a) (+1)	a) (+1)	a) (+1)	c) (0)	a) (+1)
b) Drawn from a different source					
c) No description of the derivation of the non exposed group					

3) Ascertainment of exposure					
a) Secured record (e.g. biomarkers)					
b) Structured interview or questionnaire	b) (+1)	b) (+1)	a) (+1)	a) (+1)	a) (+1)
C) Written self report					
d) No description					
<b>Confounder</b>					
1) Comparability of groups on the basis of the design or analysis					
a) Study controls for age and education	b) (+1)	b) (+1)	b) (+1)	- (0)	a) (+1)
b) Study controls for any additional factor (e.g. alcohol consumption, smoking, and first language)					
<b>Outcome</b>					
1) Assessment of outcome					
a) Independent blind assessment	b) (+1)	c) (0)	a) (+1)	d) (0)	a) (+1)
b) Record linkage					
c) Self report					
d) No description					
Overall Score	5/5 Very Good	4/5 Good	4/5 Good	1/5 Unsatisfactory	5/5 Very Good

Continued...

Table1 Continued

	Rothlein et al 2006	Srivastava et al 2000	Steenland et al 2000	Stephens et al 1995	Stephens et al 1996	Stephens et al 2004
<b>Selection</b>						
1) Representativeness of the exposed group						
a) Truly representative of the average farmers or pesticides applicators in the community						
b) Somewhat representative of the average or pesticides applicators in the community	b) (+1)	c) (0)	a) (+1)	a) (+1)	a) (+1)	a) (+1)
c) Selected group of users						
d) No description of the derivation of the group						

2) Selection of the non exposed group						
a) Drawn from the same community as the exposed group	a) (+1)	a) (+1)	a) (+1)	a) (+1)	a) (+1)	a) (+1)
b) Drawn from a different source						
c) No description of the derivation of the non exposed group						
3) Ascertainment of exposure						
a) Secured record (e.g. biomarkers)						
b) Structured interview or questionnaire	b) (+1)	a) (+1)	a) (+1)	c) (0)	a) (+1)	b) (+1)
C) Written self report						
d) No description						
<b>Confounder</b>						
1) Comparability of groups on the basis of the design or analysis						
a) Study controls for age and education	a) (+1)	- (0)	b) (+1)	b) (+1)	b) (+1)	- (0)
b) Study controls for any additional factor (e.g. alcohol consumption, smoking, and first language)						
<b>Outcome</b>						
1) Assessment of outcome						
a) Independent blind assessment	b) (+1)	d) (0)	a) (+1)	b) (+1)	d) (0)	b) (+1)
b) Record linkage						
c) Self report						
d) No description						
Overall Score	5/5 Very good	2/5 Unsatisfactory	5/5 Very Good	4/5 Good	4/5 Good	4/5 Good

**Table2 Quality Appraisal (Cohort Studies)**

	Albers et al 2004	Bazylewic z-Walczak et al 1999	Daniell et al 1992	Ohayo-Mit oko et al 2000	Misra et al 1985	Ross et al 2010
<b>Selection</b>						
1) Representativeness of the exposed cohort						
a) Truly representative of the average farmers or pesticides applicators in the community						
b) Somewhat representative of the average or pesticides applicators in the community	c) (0)	c) (0)	a) (+1)	b) (+1)	c) (0)	a) (+1)
c) Selected group of users						
d) No description of the derivation of the cohort						
2) Selection of the non exposed cohort						
a) Drawn from the same community as the exposed cohort						
b) Drawn from a different source	b) (0)	a) (+1)	b) (0)	a) (+1)	b) (0)	b) (0)
c) No description of the derivation of the non exposed cohort						
3) Ascertainment of exposure						
a) Secured record (e.g. biomarkers)						
b) Structured interview or questionnaire	a) (+1)	a) (+1)	a) (+1)	b) (+1)	a) (+1)	b) (+1)
c) Written self report						
d) No description						
4) Demonstration that outcome of interest was not present at start of study						
a) Yes	a) (+1)	a) (+1)	a) (+1)	a) (+1)	a) (+1)	a) (+1)
b) No						
<b>Confounders</b>						
1) Comparability of groups on the basis of the design or analysis						
a) Study controls for age and education	- (0)	a) (+1)	b) (+1)	- (0)	a) (+1)	a) (+1)
b) Study controls for any additional factor (e.g. alcohol consumption,						



smoking, and first language)						
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Table2 Continued

<b>Outcome</b>						
1) Assessment of outcome						
a) Independent blind assessment	b) (+1)	d) (0)	d) (0)	c) (0)	d) (0)	d) (0)
b) Record linkage						
c) Self report						
d) No description						
2) Was follow-up long enough for outcomes to occur						
a) Yes (select adequate follow up period for outcome of interest)	b) (0)	b) (0)	b) (0)	b) (0)	b) (0)	a) (+1)
b) No						
3) Adequacy of follow up of cohorts						
a) Complete follow up-all subjects accounted for	b) (+1)	a) (+1)	a) (+1)	c) (0)	d) (0)	d) (0)
b) Subjects lost to follow up unlikely to introduce bias- small number lost- >70% follow up, or description provided of those lost						
c) Follow up rate<70% and no description of those lost						
d) No statement						
Overall Score	4/8 Satisfactory	5/8 Good	5/8 Good	4/8 Satisfactory	3/8 Unsatisfactory	5/8 Good

**Table3 Quality Appraisal (Case-control Studies)**

<b>Selection</b>	Beseler et al 2006
1) Is the case definition adequate?	b) (0)
a) Yes, with independent validation	
b) Yes, e.g. record linkage or based on self reports C) No description	
2) Representativeness of the cases	a) (+1)
a) Consecutive or obviously representative series of cases b) Potential for selection biases or not stated	
3) Selection of Controls	a) (+1)
a) Community controls b) Hospital controls C) No description	
4) Definition of Controls	
a) No history of disease (endpoint) b) No description of source	a) (+1)
<b>Confounders</b>	b) (+1)
1) Comparability of cases and controls on the basis of design or analysis	
a) Study control for age and education b) Study controls for any additional factor	
<b>Exposure</b>	d) (0)
1) Ascertainment of exposure	
a) Secure record(biomarkers) b)Structured interview where blind to case/control status c) Interview not blinded to case/control status d) Written self report or medical record only	

e) No description

Continued...

Table3 Continued

2) Same method of ascertainment for cases and controls	a) Yes
a) Yes b) No	
3) Non-response rate	b) (0)
a) Same rate for both groups b) Non respondents described c) Rate different and no designation	
Overall Score	
	5/8 Good

