APPENDIX 14F: CLINICAL EVIDENCE –STUDY CHARACTERISTICS TABLES: ADVERSE EVENTS ASSOCIATED WITH INTERVENTIONS

1.1 CHARACTERISTICS OF INCLUDED PHARMACOLOGICAL INTERVENTION STUDIES

1.1.1 CAMPBELL1978

Study ID	CAMPBELL1978
Bibliographic reference	Campbell M, Anderson LT, Meier M, Cohen IL, Small AM, Samit C, et al. A comparison of haloperidol and behavior therapy and their interaction in autistic children. Journal of the American Academy of Child Psychiatry. 1978;17:640-655.
Methods	**Allocation:** Randomised **Matching:** No matching **Blindness:** Participants, intervention administrators, parents and outcome assessors were blind to group assignment **Setting:** Inpatient **Raters:** Not reported **Country:** USA
Participants	**Diagnosis:** Early infantile autism **Coexisting conditions:** 12.5% mild LD; 20% moderate LD; 27.5% severe LD; 35% profound LD **Qualifying Diagnostic Assessment:** Diagnosis was made independently by two research psychiatrists. In 50% of the sample, a third psychiatrist also diagnosed the children on the basis of the criteria of the British working party (Creak, 1964) **N:** 42 (42 randomised, but 2 dropped out and demographics and data analysis only reported for N=40) **Age:** 2.6-7.2 years (mean: 4.5 years) **Sex:** 20% female **Ethnicity:** Not reported **IQ:** Not reported **Inclusion criteria:** Not reported **Exclusion criteria:** Participants with a history of seizure disorders, gross neurological deficit, endocrine or systemic disease, or an identifiable cause for autism were excluded
Interventions	**Experimental Intervention: Haloperidol** or placebo were delivered together with 7 weeks of behaviour-based therapy which used operant methodologies and targeted language acquisition. **Delivery of intervention:** Haloperidol was administered by the research nurse (behaviour therapy was delivered by therapists, with no further detail reported) **Format or method of administration:** Oral tablet administration **Intensity:** 0.5mg-4mg/day (mean: 1.65mg/day) for haloperidol; 2-4mg/day (mean: 3.95mg/day) for placebo **Duration of intervention:** 8 weeks for drug treatment **Total duration of follow-up:** 12 weeks (including 2 week placebo washout at the beginning and 2 weeks of placebo and behaviour therapy at the end of the trial)

Outcomes	Outcomes were reported for clinical efficacy. However, as no measure of variability was reported, data could not be extracted. The only outcome reported with extractable data was: **Adverse events** (as measured by a dichotomous measure of 'any side effect'. The most common side effect for haloperidol was excessive sedation)
Study Design	RCT
Source of funding	Public Health Service Grant MH 04665 from the National lnstitute of Mental Health and McNeil Laboratories
Limitations	1. High risk of selection bias due to unclear randomisation method and insufficient detail reported with regards to allocation concealment. There was also no examination of potential pre-intervention group differences and thus group comparability was unclear 2. High risk of selective reporting bias as the trial is not registered so the full outcomes tested is unclear. Furthermore, the clinical efficacy data is not reported in sufficient detail to be entered into a meta-analysis as no measure of variability is reported 3. High risk of other bias as the age of the study may shed doubt on applicability. In addition, funding was received from the pharmaceutical company that manufactured the drug tested raising concerns with regards to conflict of interest
Notes	Clinical efficacy data could not be extracted from the study as no measure of variability was reported.

1.2 CHARACTERISTICS OF EXCLUDED PHARMACOLOGICAL INTERVENTION STUDIES

1.2.1 CACCIA2011

Reason for exclusion	Systematic review with no new useable data and any meta-analysis results not appropriate to extract

1.2.1 CAMPBELL1997

Reason for exclusion	Safety data cannot be extracted as outcomes only reported for experimental and not control group

1.2.1 ROKE2009

Reason for exclusion	Systematic review with no new useable data and any meta-analysis results not appropriate to extract

1.2.2 RUPPRISPERIDONE2001 (AMAN2005)

Reason for exclusion	Safety data cannot be extracted. Author contacted to request results but no reply

1.3 REFERENCES OF EXCLUDED PHARMACOLOGICAL INTERVENTION STUDIES

Aman MG, Arnold LE, McDougle CJ, Vitiello B, Scahill L, Davies M, et al. Acute and long-term safety and tolerability of risperidone in children with autism. Journal of Child and Adolescent Psychopharmacology. 2005;15:869-884.

Caccia S, Clavenna A, Bonati M. Antipsychotic drug toxicology in children. Expert Opinion on Drug Metabolism and Toxicology. 2011;7:591-608.

Campbell M, Armenteros JL, Malone RP, Adams PB, Eisenberg ZW, Overall JE. Neuroleptic-related dyskinesias in autistic children: a prospective, longitudinal study. Journal of the American Academy of Child and Adolescent Psychiatry. 1997;36:835-843.

Roke Y, van Harten PN, Boot AM, Buitelaar JK. Antipsychotic medication in children and adolescents: a descriptive review of the effects on prolactin level and associated side effects. Journal of Child and Adolescent Psychopharmacology. 2009;19:403-414.