These results are supplied for informational purposes only.
Prescribing decisions should be made based on the approved package insert in the country of prescription

Sponsor/company:	sanofi-aventis	**ClinialTrials.gov Identifier:**	NCT00434681
		Study Code:	PARAC_L_00859
Generic drug name:	Paracetamol	**Date:**	26/Feb/2008

Study title:
Non-comparative, open-label, multicentre study of the acceptability and tolerability of 4.8% paediatric paracetamol oral suspension

Investigators :
15 paediatricians or general practitioners practicing in private offices, in France.
Coordinating investigator: Dr Jean LALAU KERALY – PARIS XVI.

Publication : Not applicable

Study duration:
Date of first inclusion: October 30, 2006
Date of last inclusion: January 27, 2007

Development phase IIIb

Objectives:
Primary objective:
To evaluate the acceptability over 24 hours of a new paracetamol formulation,
4.8% paediatric oral suspension in children weighing between 3 and 26 kg inclusive
Secondary objectives:
Evaluate the general tolerability of treatment

Design:
Non-comparative open-label, multicentre, phase IIIb study of the acceptability of paediatric 4.8% paracetamol oral suspension in children prescribed antipyretic and /or analgesic treatment with paracetamol over a minimum period of 24 hours.

Number of patients:
Planned: 48 children.
Included: 55 patients
ITT : 55 patients
PP: 55 patients
Tolerability: 55 patients

Diagnosis and inclusion criteria:
- Child of either sex, weighing between 3 and 26 kg (included) presenting fever and/or pain justifying treatment by paracetamol for a minimum duration of 24 hours.
- May be followed up throughout the study period on an outpatient basis.
- Informed consent obtained in writing from parents, legal guardian or from the child him/herself if sufficiently old.

Exclusion criteria:

- Patient with gastrointestinal disorders, vomiting.
- Hypersensitivity to paracetamol or to one of the components of the study medication
- Hepatic insufficiency.
- Fructose intolerance
- Serious concomitant disease such as cancer, immune deficiency or a serious renal, hepatic, cardiac, neurological, psychiatric or metabolic disease.
- Significant history of laboratory abnormalities.
- Treated by Kayexalate®
- Not benefiting from the social security system
- Parents incapable of understanding.
- Unable to return for the final evaluation and/or comply with the constraints of the study.
- Participation in another clinical study during the 30 days before inclusion
- Close relative of the investigator

Study product:

- Active ingredient: Paracetamol
- Pharmaceutical form: Sugar-free, paediatric, oral suspension
- Dosage strength : 4.8%
- Route of administration: Orally, either pure, or diluted in a small quantity of drink
- Dosage: 60 mg/kg/day. The presentation is adjusted for administration 4 times daily, i.e. approximately 15 mg/kg/6 hours
- Duration of prescription: 24h, if the investigator wants to continue treatment he/she must prescribe marketed paracetamol

Reference product:

Not applicable

Endpoints:

Primary endpoint:

Global assessment of treatment by parents, guardian or childminder, measured using a 4-level semi-quantitative scale (very acceptable, acceptable, indifferent, refusal), over 24 hours (4 evaluations at 6-hour intervals).

Secondary endpoints

Global assessment by the child (from 3 years), using a Hedonic Visual Scale during last dose before visit V2

Tolerability:

Events reported by the child, parents or legal guardian during visit V2
Events collected in the child's diary
Events noted by the investigator during Visit 2

Statistical methods:

Primary analysis: Per protocol population (PP).
Determination of the 80% two-sided confidence interval of the proportion of patients finding treatment unacceptable (rounded mean of the 4 evaluations > 1). Treatment is considered to be acceptable if this interval excludes 25% and contains 10% or if the upper limit of the interval is < 10%.
Descriptive statistics for the hedonic visual scale and safety

SUMMARY:

Fifty-five patients were included by 11 investigators. All patients took at least one dose of the study treatment. No major deviation from the protocol was identified.

Thirty-nine patients terminated the study according to the protocol, 16 prematurely discontinued the study including 7 who refused treatment and 9 in whom the fever did not persist. Treatment discontinuations were taken into account for the evaluation of acceptability.

The 3 populations analyzed (tolerability, ITT and PP) were identical and comprised the 55 included patients.

There were 30 boys (54.5 %) and 25 girls (45.5 %), aged on average 3.3 ± 1.9 years (mean ± SD), 31 children (56.4 %) were aged 3 years or more They weighed 14.5 ± 4.8 kg for a mean height of 93.8 ± 16.4 cm, i.e. a mean body mass index of 16.3 ± 2.5 kg/m².

Prescription of paracetamol was justified by a fever for 54 patients (98.2%) (Including 24 with concomitant pain), and pain for 25 patients (45.5%) (Including 24 with concomitant fever).

39 patients (70.9 %) took the 4 doses of treatment planned in the protocol, 6 patients (10.9 %) only took 3 doses, 7 patients (12.7%) 2 doses and 3 patients (5.5 %) only a single dose.

ACCEPTABILITY

Treatment was considered to be globally acceptable for 47 patients (85.5 %) and unacceptable for the 8 others (14.5 %). The 80 % two-sided confidence interval of the percentage of patients for whom treatment was considered to be unacceptable was [8.7 %; 22.6 %]. This did not reach 25%, the threshold defined a priori as "intolerable" but, on the contrary, included 10% the expected threshold of non-acceptability. Consequently, 4.8% paracetamol oral suspension was considered to be acceptable by

the patients.

The mean acceptability score over 24 hours was 2.14 ± 0.92 (on a scale ranging from 0 = refusal to 3= very acceptable), and for all 191 evaluations, treatment was considered to be "acceptable" 176 times (92.1 %).

For the 31 children aged 3 years or more in whom the hedonic visual scale was applied, 44.4 % considered the treatment to be "not good" (80 % two-sided CI [31.1 %; 58.5 %])

TOLERABILITY:

No serious or unexpected adverse event or any treatment-related event was reported.

A single intercurrent event was reported during the study: "Vomiting of food", of moderate severity, not related to treatment according to the investigator.

Date of report: 25 May 2007