Safety evaluation of a whey protein fraction containing a concentrated amount of naturally occurring TGF-β2

Roy Forster 1, Michel Bourtourault 2, Yong Joo Chung 3, Jérémy Silvano 1, Guillaume Sire 1, François Spezia 1, Caroline Puel 2, Jacques Descotes 1, Takashi Mikogami 1

Atlanbio
+33 (0)1 51 10 01 00
atlanbio@atlanbio.com
www.atlanbio.com
1 Rue Graham Bell - Z.I. de Brais
B.P. 40309,
44605 Saint Nazaire Cedex, France

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CiToxLAB in Denmark
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contact.denmark@citoxlab.com
Hestehavevej 36A, Elbjy,
DK-4623 Lille Skensved, Denmark

CiToxLAB in Hungary
+36 88 545 300
contact.hungary@citoxlab.com
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ALSO REPRESENTED BY
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customerservice@cron.co.kr
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Yeongtong-gu, Suwon-si - Gyunggi-do,
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**INTRODUCTION**

TGF-β2 is a whey protein isolate derived from cow milk, containing a concentrated amount of transforming growth factor β2 (TGF-β2). It is intended for nutritional use in infants and adults. The importance of TGF-β in milk, where it participates in the prevention of allergy by inhibition of immunological tolerance in the first weeks of life, has been repeatedly demonstrated (Ando et al., 2007; Nakao, 2010; Oddy and Rosales, 2010; Rautava et al., 2011(1, 2, 3, 4). TGF-β is a multifunctional protein, playing an important role in embryonic development, differentiation and control of cellular multiplication, tissue repair and bone and cartilage formation. TGF-β2000p commercial name: Vatalarmor® GF-100) is a dietetic ingredient produced with commonly used technology in the dairy industry. Its major protein component is lactoferrin and lactoperoxidase. It contains other minor protein components such as secretory component (part of polymeric immunoglobulin receptor), complement factor C3 and lactophorin (glyCAM-1). TGF-β is also part of this protein isolate, in higher concentration than that found in unprocessed cow milk on a dry matter or protein basis.

**MATERIALS AND METHODS**

We performed a 13-week oral rat toxicity study (OECD 408), and as the proposed applications for TMD060p may be used as an ingredient in infant formula we also performed a 6-week juvenile rat study based on the FDA Guidance, Nonclinical Safety Evaluation of Pediatric Drug Products. In vitro bacterial reverse mutation test and in an in vitro micronucleus test. Based on 13-week oral toxicity study and 6-week juvenile toxicity study in rats and the in vitro bacterial reverse mutation test and the in vitro micronucleus test. Based on 13-week oral toxicity study and 6-week juvenile toxicity study in rats and the in vitro bacterial reverse mutation test and the in vitro micronucleus test.

**RESULTS**

Body weight was unaffected in the 13-week study (Figure 1). In the juvenile study, a transitory and reversible effect on body weight (Figure 2) during the pre-weaning period was without any evident harmful consequences, and was considered to result from interference by the TMD060p treatment with the nutritional benefits of the dams’ milk (through viscosity, physical obstruction or effects on satiety). There were no changes at ophthalmology or clinical signs indicative of toxicity in either study. No behavioral alterations or CNS effects were seen in the FOB study (Table 3). Pre-weaning development milestones, puperal reproductive markers, learning and memory functions were unaffected.

**CONCLUSION**

Based on 13-week oral toxicity study and 6-week juvenile toxicity study in rats and the in vitro bacterial reverse mutation test and the in vitro micronucleus test, we can conclude that these studies, which covered a wide variety of endpoints, support the safety of TMD060p, a whey protein isolate concentrated in TGF-β2. A NOAEL of 2000 mg/kg/day in adult rats (highest level tested) and of 600 mg/kg/day in rat pups (only level tested) was established.

**BIBLIOGRAPHY**


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