TRANSLATED FROM RUSSIA

RESEARCH OF THE SENSITIZING ACTION

1. The sensitizing activity of the material was researched in accordance with GOST R ISO 10993.10-99 "Medical devices. Study of biological action of medical devices. Part 10. Research of irritating and sensitizing action. Supplement F. Research of sensitizing action on white rats".

The experimental animals were kept in accordance with GOST R ISO 10993.2-99 "Medical devices. Study of biological action of medical devices. Part 2. Regulations on protection of animals".

Samples
The material is submitted in a sterile form. "ARGIFORM" is filled in disposable injection plastic syringes, which are tipped and vacuum-sealed in individual blister packaging. Each set consisting of a blister packaging with a syringe and an injection cannula which are packed into a separate branded carton box. The marking, description and the trademark are printed on boxes.

2. Description and results of the research

The possible allergenic action of the "ARGIFORM" material was studied in experiments on male white rats using subcutaneous injection with application of provocative intracutaneous test and conduction of a serologic diagnostic reaction with blood serum with the purpose to reveal the existence of the complex 'antigen-antibody', according to the degranulation reaction of fat cells (DRFC). Additionally, the mass coefficient of the immunocompetent organs of thymus and spleen and their correlation were determined during sensitizing action study.

On the 16^{th} day after the subcutaneous injection of the material to the experimental rats a provocative skin test was done: 0.02 ml of a newly-prepared extract from the material was injected to the experimental rats intradermally (and the same amount of medium to the control animals) in the area of animals' depilated flanks.

The observation of the animals in 30 min after injecting of the permissible dose, in 24 or 48 hours, i.e. at the 17^{th} or 18^{th} days of experiment did not reveal any late reaction – of hypersensibility.
An immunologic degranulation reaction of fat cells was done, and its results also showed an absence of sensitizing action of the material: the percentage of degranulation of fat cells amounted to 6.4 (when a degranulation of 10-15% is considered to be a weak reaction).
Overall analysis of sensitizing action of the material showed: a negative provocative skin test, absence of differences of the weight coefficients of thymus

and spleen and thymus/ spleen ratio between control and tested groups, so we may come to the conclusion that material of this implant was not allergenic.

At the prosection of tested animals, there weren't macroscopically revealed any differences of internal organs and tissues from the control. The weight coefficients of the internals have neither any statistically reliable difference (table #1).

Table #1
Body mass and weight coefficients of the internal organs of rats during the study of sensitizing action of the material

Indices	Control	Experiment	P
Body mass, g	262.000±2.906	268.000±2.708	> 0.05
Internal organs, mg:			
- thymus	1.063±0.069	1.150±0.046	> 0.05
- liver	27.176±0.738	28.112±0.370	> 0.05
- thymus/spleen	0.350±0.040	0.340±0.021	> 0.05
- spleen	3.201±0.180	3.439±0.131	> 0.05
- kidneys	6.220±0.079	6.315±0.098	> 0.05
- testicles	10.224±0.363	10.347±0.233	> 0.05

3. Conclusion on the sensitizing action

Analyzing all factors on which the sensitizing action testing of the material was based:

- a negative provocative skin test,
- an absence of differences from the control of weight coefficients of thymus gland and the spleen,
- the thymus/spleen mass ratio,

we may come to the conclusion that the material is not allergenic.

At the other side, factors which shows the hypersensibility of tested material are:

- a leucocytosis (eosinophilia) of the peripheral blood,
- a shift of the blood serum protein formula towards an increase of globulins level,
- an increase of the histamine content and 17-ketosteroids.

As it follows from the above-mentioned results of examination of all the animal species on which the toxicity of material "ARGIFORM" was studied, none of those indices differed from the control, which may also serve as confirmation of absence of sensitizing effect of the material.

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