

Biocidal Products Committee (BPC)

Opinion on a request according to Article 75(1)(g) of Regulation
(EU) No 528/2012 on the

**Status of copper sulphate pentahydrate in Manica Spa and
Stoermoellen product Stalosan F for product type 3**

ECHA/BPC/176/2017

Adopted

11 December 2017

Opinion of the Biocidal Products Committee

on the status of copper sulphate pentahydrate in Manica Spa and Stoermoellen product Stalosan F

In accordance with Article 75(1)(g) of Regulation (EU) No 528/2012 of the European Parliament and of the Council 22 May 2012 concerning the making available on the market and use of biocidal products (BPR), the Biocidal Products Committee (BPC) has adopted this opinion on the status of copper sulphate pentahydrate in the product Stalosan F for product type 3.

This document presents the opinion adopted by the BPC, having regard to the conclusions of the rapporteur.

Process for the adoption of opinions

A request from the Commission was received by ECHA on 8 February 2017. The BPC members appointed the rapporteur at the BPC-19 meeting of 1-3 March 2017. The rapporteur presented the draft opinion to the BPC-23 meeting of 11 – 14 December 2017.

Following the adoption of the opinion at BPC-23, the opinion was amended and finalized according to the outcome of the discussion.

Adoption of the opinion

Rapporteur: France

The BPC opinion was adopted by consensus on 11 December 2017. The opinion is published on the ECHA webpage at:

<https://echa.europa.eu/regulations/biocidal-products-regulation/approval-of-active-substances/bpc-opinions-on-other-requests-under-the-biocidal-products-regulation>.

1. Further details of the opinion and background

1.1 Request for the opinion and background

On 22 February 2016 and 30 September 2016, Manica Spa and Stormoellen submitted respectively declarations of interest under Article 15(a) of Regulation (EU) No 1062/2014 to notify the active substance Copper sulphate pentahydrate (EC 231-847-6, CAS 7758-99-8) for use in biocidal products of product-type 3 (PT3).

In the declaration Manica Spa and Stormoellen argue that the product Stalosan F contains copper sulphate pentahydrate acting as an inhibitor of the microbial enzyme urease to control the production of ammonia resulting from the action of urease on urea. They argue that it has an indirect effect on bacteria, and that indirect effects were considered out of the scope of the Biocidal Product Directive 98/8/EC until the European Court's ruling in case C-420/10 Söll v Tetra GbH¹.

Copper sulphate pentahydrate was not notified in the review programme for product-type 3. However, copper sulphate pentahydrate was notified in 2003 and included in the review programme as an active substance for product-type 2. The application for approval was submitted by Manica Spa in 2007 resulting in an approval as an active substance for use in biocidal product of product-type 2 by Regulation (EU) No 1033/2013 of 24 October 2013.

Discussions took place during the 65th and 66th CA meetings of representatives of Member States Competent Authorities for the implementation of Regulation (EU) No 528/2012 of September and November 2016 concerning the acceptance of the declarations of interest to notify².

During the discussions it appeared that further technical input was needed in order to be able to conclude on this case, in particular to know if in the product Stalosan F referred to by Manica and Stormoellen, copper sulphate is acting as an active substance or not. It was agreed that the Commission will request a formal opinion to ECHA in order to help the decision making process on the acceptance or rejection of the declarations of interest to notify.

Therefore, the Commission has requested ECHA to formulate an opinion via the BPC on the following questions:

- (a) Does copper sulphate pentahydrate act as an active substance in the product Stalosan F referred to by Manica Spa and Stormoellen for product-type 3?
- (b) If it acts as an active substance :
 - 1. What is the mode of action of copper sulphate in the product Stalosan F?
 - 2. Is this the same mode of action as for copper sulphate used in PT2 biocidal products, which was notified in 2003 and already approved by Regulation (EU) No 1033/2013?
 - 3. Is this the same mode of action as other active substances notified and included in the review programme in 2003 for PT3, and currently under review or already approved?

¹ <http://curia.europa.eu/juris/liste.jsf?num=C-420/10&language=EN>

² [CA-Nov16-Doc.5.7 - Restricted - DoI - Draft conclusions.docx](#)

1.2 Summary of information supporting the request for the opinion

The company provided :

1. a supporting document describing the function of copper sulphate pentahydrate in the product Stalosan F.

The veterinary hygiene product Stalosan F is a disinfectant (0.25 % w/w chloramine T and also 1.5 % w/w copper sulphate pentahydrate) for the protection of hard surfaces and bedding used in livestock housing and for the control of ammonia. Stalosan F contains the active ingredient chloramine T as a broad spectrum disinfectant. Chlorine from chloramine T attacks lipids in bacterial cell walls and membrane, leading to rapid cell lysis and death. Upon lysis of the cells, intracellular enzymes such as urease are released. These enzymes may become bound to organic matter and clay minerals, thereby protecting them to breakdown by extracellular proteases. In this way, extracellular urease released from lysed bacteria can remain active and fully functional for extended periods.

Bedding in animal housing contains large amount of urine and hence high levels of urea. When urea comes into contact with extracellular urease the following reaction is catalyzed:



Urease drives this reaction by promoting the production of ammonia.

The high levels of ammonia associated with livestock production are an increasing cause for concern on grounds of both animal welfare and environmental impact. Any measures that lead to a reduction in ammonia production are therefore highly desirable.

The product Stalosan F achieves this in two ways: through the neutralization of existing alkaline ammonia by mineral acids such as acidic phosphates and sulphates and by the inclusion of copper sulphate pentahydrate in the formulation. Copper sulphate pentahydrate acts as an inhibitor of extracellular urease, thereby reducing the production of ammonia by the action of this enzyme on urea. As this process occurs outside the bacterial cells, it is considered to be an indirect effect. The copper sulphate pentahydrate present in Stalosan F is not intended to have a direct disinfectant effect on bacteria, neither killing them, nor inhibiting their growth.

Studies have shown that the cupric ion (Cu^{2+}) is a much more potent inhibitor of urease than the cuprous ion of copper sulphate pentahydrate. Consequently, Fe^{2+} is also included in Stalosan F as a reducing agent. In the presence of water, this leads to the reduction of Cu^{2+} to soluble Cu^+ as a result of the following reaction: $\text{Cu}^{2+} + \text{Fe}^{2+} \rightarrow \text{Cu}^+ + \text{Fe}^{3+}$. Although the mechanisms of urease inhibition is not yet fully understood, it is thought to involve the reaction of copper ions with a sulphhydryl group in the active center of the enzyme in a reaction analogous to the formation of metal sulphides.

2. An efficacy study according to EN 13697 method (contact time of 30 min, at 20-25 °C, without soiling) on *Salmonella thyphimurium* comparing the efficacy of Stalosan F including copper with the efficacy of Stalosan F excluding copper:

	Stalosan F including copper	Stalosan F excluding copper
Exposure time	Average % kill	
30 minutes	99.9840 %	99.9570 %

Results from this study showed no biocidal activity of copper sulfate pentahydrate in the product of Stalosan F according to the tested conditions (contact time of 30 minutes, at 20-25 °C without soiling), since both products showed similar efficacy and achieved about a 4 log reduction of bacteria.

3. An efficacy study according to EN 1656 method (contact time of 30 min, at 10 °C, with dirty conditions) on bacteria with the product Stalosan F at 20 % v/v (minus copper sulphate pentahydrate). This study was requested following a discussion at the BPC Efficacy Working Group on 31 May – 1 June 2017 (Final minutes - WGIII2017_EFF_6-7_Copper sulphate pentahydrate – PT 3). The proposed approach is considered to be in the line with the section “Co-formulant(s) being a potential active substance in disinfectant products (WGII2017)” of the document “Technical Agreements for Biocides”.

According to the results, the product Stalosan F (minus copper sulphate pentahydrate) achieved a reduction in a bacterial population of ≥ 5 orders of magnitude within 30 minutes at 10 °C in dirty conditions (10 g/L BSA + 10 g/L yeast extract).

1.3 Evaluation of information supporting the request for the opinion

- (a) Does copper sulphate pentahydrate act as an active substance in the product Stalosan F referred to by Manica Spa and Stormoellen for product-type 3?

The applicant provided some justifications to demonstrate that in the product Stalosan F copper sulphate pentahydrate should be considered as a co-formulant: its primary function is to reduce the production of ammonia by inhibition of urease, produced consequently to the action of the active substance chloramine T.

An efficacy test on *Salmonella thyphimurium* has been provided to justify the non-activity of copper sulphate pentahydrate. This target organism is relevant for PT 3 uses but does not presume of the basic bactericidal activity of copper sulphate pentahydrate in the product Stalosan F (the study performed by the applicant on *Salmonella thyphimurium* was not sufficient to conclude whether copper sulphate pentahydrate acts as an active substance in the product Stalosan F, especially in relation to soiling conditions and target organisms). Nevertheless, it has to be noted that the copper sulphate pentahydrate concentration in the product Stalosan F (1.5 % w/w equal to 10 g/L as a ready to use product) is less than the one tested according to EN 1040 (14 g/L), showing the bactericidal innate efficacy of copper sulphate pentahydrate for uses in PT 2.

Moreover, following discussions at the BPC Efficacy Working Group on 31 May – 1 June 2017, the EFF WG agreed that additional efficacy test should be performed. The product Stalosan F should be tested without copper sulphate pentahydrate and with appropriate soiling, temperature and contact time for the intended use (dirty conditions relevant for PT3). The study carried out according to EN 1656 demonstrated that without copper sulphate pentahydrate, the product Stalosan F is able of producing the required biocidal effect under normal use conditions.

As copper sulphate pentahydrate does not act as an active substance in the product Stalosan F referred to by Manica Spa and Stormoellen for product-type 3 question (b) mentioned in section 3.1 has not been considered.

2. Overall conclusions

Copper sulphate pentahydrate present in the product Stalosan F used as a disinfectant for veterinary hygiene (PT 3) shall not be regarded as an active substance.

3. References

- Declarations of Interests to notify from Manica of 2 February 2016 and 30 September 2016, and from Stormoellen of 30 September 2016.
- Safety data sheet of the product Stalosan F.
- Technical report - CH 691/2016 "Stalosan F dry disinfectant: antimicrobial activity against *Salmonella* Thyphimurium", Colombo S.
- Study report IMSL2017/06/009.3.3 "Activity of Stalosan F (minus copper sulphate pentahydrate) against *Proteus vulgaris*, *Staphylococcus aureus* and *Enterococcus hirae* using a method based on the European Disinfection Test EN1656:2009", 15 August 2017.