

ZEROGERM

IDENTIFICATION AND CHARACTERISTICS OF THE PRODUCT

ZEROG3RM[®] looks like a large pellet 700 grs block and each block contains 35% pure paraformaldehyde stupported in special ingredients.

The disinfectant power of ZEROG3RM[®] is very high and the product has also a well known action as a potent bactericide, fungicide and virucide.

ZEROG3RM[®] is an active agent against: colibacillus, salmonellae, streptococcus, staphilococcus, pneumococcus, brucellae, shigellae, pasteurellae, proteus and also moulds and virus.

These bacteria are immediatly killed by the action of formaldehyde gas. However, during the practice of disinfection, the time of contact between the bacteria and the gas is longer than necessary, in order to allow the gas saturation of the place.

The concentration of formaldehyde necessary to obtain a disinfecting action varies according to the period of contact of the gas in the room and the objects to disinfect. One block of ZEROG3RM® is needed for 100/400 m3 of premises according to the sector of utilization. Each block of ZEROG3RM® must be placed on a metallic tray or on a heat-resistant material. When the flame spread all over the block, it has to be extinguished by covering for a few seconds: a slow flameless combustion has begun.

Thus a constant emission of formaldehyde gas is obtained for about 3 hours. The strong and lasting bactericide power and the innocuity for most of the materials make the application of ZEROG3RM® very rapid and simple.

CHEMICAL-PHYSICAL CHARACTERISTICS

Main Characteristics of the active principle

The active principle is paraformaldehyde; it is obtained by polymerisation of formaldehyde.

Chemical-physical data:

The active principle is a white powder with a not so clear crystal structure and with a typical smell of formaldehyde (pungent smell of formic aldehyde at warm temperature).

Melting Point: 163°-172°C. It sublimes just before 100°C until to 180°-200°C.

It completly depolymerizes in formic aldehyde.

Solubility in water and organic solvents (at 20°-25°C): it is almost insoluble in cold water, alcohol and ether.

Flash Point: 70°C Fire Point: 300°C

Explosive and burning properties: there is not so much fire ranger, only if heat and flame are present. There isn't self-ignition danger.

Stability during storage: the compound is absolutely stable and only by heating it develops formaldehyde gas and carbon oxides; it can react with oxidant compounds.

Chemical-physical characteristics of the ended product ZEROG3RM®

It is a round pellet with 15 cm diameter, 4 cm gage and 700 grs weight; the color is gray-green- light brown and the smell is characteristic of formaldehyde.

Composition: Paraformaldehyde: 35% Excipients: 65% Apparent density (indicatively): 0,97 Kg/dm3 Acidity: 40 mg KOH/grs product Fire danger only during flame exposition. The product is not corrosive.

No teorical limit expiration date: in normal condition of temperature and humidity the product doesn't change its chemical-physical characteristics.

STUDY ON THE EFFICACY OF THE PRODUCT

The action of ZEROG3RM® is obtained by its flameless combustion, so that formaldehyde is released slowly and consistently without dispersive secondary reactions. On the consequence this product doesn't present the well known difficulties coming from liquid formaline and from its polymers. Infact from liquid formaline the production of formaldehyde gas is obtained by means of exotermic reactions or by heating.

The formalin-potassium permanganate reaction is commonly used for the disinfection of premises (Medicamenta, Vol. II, page 1521); the oxidizing agent transforms part of the formaldehyde in to formic acid with a strong emission of heat that releases the remaning formaldehyde from the aqueous solution. Therefore, while a part of formaldehyde is released with a tumultuous production of gas, that carries out its disinfecting action, the other part becomes oxidized and is therefore useless. On the contrary, the formulation of ZEROG3RM® allows to use more than 94% of formaldehyde without loosing it and without dangerous dispersive secondary reactions.

Results of tests on the efficacy of ZEROG3RM®

Formaldehyde is usually combined with permanganate of potassium to obtain an exothermic reaction. The result of this reaction produces a gas which contains formic aldehyde, that is able to destroy every harmfull micro-organism. However, during this reaction, a loss of disinfectant active substances occurs and, above all, there are emanations of carbon monoxide and carbon dioxide, that are highly toxic gases. The gas resulting from the combination formaline/permanganate is heavier than air, so it cannot spread evenly in the various spots of a building. Also, it has been scientifically verified that the formic aldehyde - created by the exothermic reaction of formaline with permanganate - becomes almost completely inert after about 32 minutes, due to a quick molecular transformation deriving from its polymerisation. On the contrary, the ZEROG3RM® , during its slow combustion process, liberates a dry gas which contains a pure formic aldehyde, totally inoffensive because there are no emissions of carbon monoxide and carbon dioxide. Such gas, absolutely anhydrous, is lighter

than the air; therefore it spreads into buildings with uniformity. Since the formic aldehyde liberated is completely dehydrated, it has a high capacity of mixing quickly and of fixing with the surrounding air oxygen, which gives as a result a more durable disinfectant effect.

As a consequence polymerisation happens only after over 6 hours; so the disinfectant power remains active for a period that is long enough to get rid of every harmfull micro-organism.

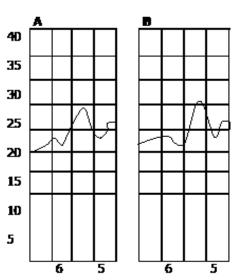
What has been briefly illustrated above proves clearly the strong efficacy of ZEROG3RM® and its practical use.

As far as economical convenience is concerned, it must be considered that: to disinfect a place of 100 m3, 3 lt of formaline are used at 33% combined with 3 Kg of permanganate of potassium, and the exothermic reaction gives about 99 grs of formic aldehyde (that remains active for about 32 minutes). to disinfect the same place of 100 m3, one block of ZEROG3RM® is required, which combustion gives 200 grs (300 lt) of formic aldehyde (that remains active for at least 6 hours).

After long and difficult researches it appears that: when analysing gases produced by the usual formaline-permanganate combination, the rate of HCHO (formaldehyde) never exceeded 11% (the reaction of 100 grs of commercial formaline-permanganate gives at the most 3,3 grs of HCHO). When analysing fumigated gases produced by ZEROG3RM®, the rate of HCHO (formaldehyde) went up to 94,5% (100 grs of ZEROG3RM® give at the most 29,3 grs of HCHO).

These tests were carried out at the Laboratories of Padova University.

The gas-chromatography's method was used for monitoring these researches.



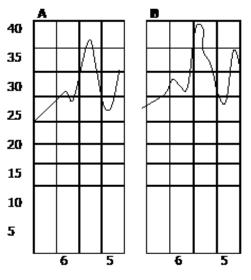
AT THE BEGINNING OF COMBUSTION

CHROMATOGRAM n°1

Datta of gases produced by one tablet of ZEROG3RM® at the beginning of its combustion: x10 x32 Ev 100 Col 54 100 gr of ZEROG3RM® give 12,44 and 18,16 gr of formaldehyde

A: the highest peak = 10x30B: the highest peak = 10x40





CHROMATOGRAM n°2

Datta of gases produced by one tablet of ZEROG3RM® during its combustion: x10 x32 Ev 100 Col 54 100 gr of ZEROG3RM® give 29,3 and 28gr of formaldehyde

A: the highest peak = 10x40

B: the highest peak = 10x40

ΤΟΧΙCΙΤΥ

The toxicity is caused by formaldehyde, which is the active principle released from combustion.

Formaldehyde is a natural substance in first place, ubiquitously present. In the atmosphere it is continuously formed by photochemical processes. This means, that as long as there are human beings on the earth, they have inhaled formaldehyde contained in the air.

Furthermore, it is produced in all combustions, being present, for example, in automobile exhaust, tobacco smoke, etc. Concentrations measured in outdoor air are shown in the following table.

AREA	CONCENTRATION IN PPM
Above the ocean	0.0001 - 0.005
In rural areas	0.001 - 0.012
In urban areas – normal circumstances	0.002 - 0.016
In urban areas – with heavy traffic	0.031 - 0.056
In pollution (Los Angeles)	0.165

Formaldehyde concentrations measured in ambient outdoor air (1 - 6)

Formaldehyde is also an essential intermediate in the metabolism of normal cells in animals and humans. All tissues permanently contain measurable amounts of formaldehyde, e.g., human blood 2-3 ppm. There is no accumulation of formaldehyde in the environment or in the human body since it is rapidly oxidized and biodegraded. In the body exogenous formaldehyde has half-life of 1,5 minutes because then it is metabolised into formic acid and carbondioxide.

The Formic Aldehyde is very toxic against micro-organism (unicellular organism); while no adverse effects on superior human organisms are known.

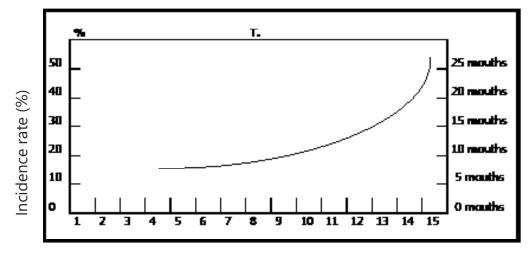
Only little irritant effects on the mucous membranes have been observed, but these symptoms disappear as soon as the formaldehyde exposure ceases. The danger coming from inhalation of formaldehyde is very little because its pungent odor is perceived even when the concentration of formaldehyde is less than 1 ppm. The left overs consist of carbonised material and inert ashes. It is not possible to find residue of Formic Aldehyde in the disinfected area; after one day of air entrainment the concentration of Formic Aldehyde is less than the maximum tolerable value in the environment: 2 ppm.

ONCOGENIC AND CANCEROGENIC POTENTIAL OF ZEROG3RM®

Animal data

In long-term studies on rodents, the inhalation of formaldehyde resulted in a significant doserelated incidence of squamous cell carcinomas of the nasal cavities in rats. In mice such nasal tumors occurred only at the highest dose level of 14,3 ppm, however, at a statistically not significant incidence rate of 1%. There was no formation of cancer tumours in hamsters. As the following figure shows, an increase of 2 ¹/₂ times of concentration of formaldehyde (from 5,6 ppm to 14,3 ppm) caused an increase of 50 times of cancer incidence in rats from 1% to almost 50%, demonstrating that the cancer mechanism strongly depends on the formaldehyde concentration.

Dose response relationship of the development of squamous cell carcinoma in rats after 2 years of formaldehyde exposure (24 months) to paraformaldehyde of ZEROG3RM®



Paraformaldehyde concentration (ppm)

Tumors occurred only at the site of initial contact and at concentrations which caused cytotoxicity and tissue destruction. Inhalation of 15 ppm formaldehyde for 6 hours per day caused ulceration of nasal mucosa of rats already after 3 days. The effects of formaldehyde depend on the concentration tissues are exposed to, but not on the cumulative dose. Mice are able to reduce their minute respiratory volume of 40 - 70 % during the exposure of formaldehyde. This resulted in a decrease of 50 % of the delivered dose at the target tissue compared to rats, thus reducing the possibility of tissue injury and subsequent tumour formation. Non-cancerous lesions of the nasal mucosa of rats and mice formed in long-term studies were reversible even after 2 years of exposure in mice at every dose level and in rats up to 5 – 6 ppm after cessation of the exposure.

Human data

No adverse effects on human health have been observed even after long and continuous exposition to ZEROG3RM[®]. Because of formaldehyde's pungent odor and its irritant effects on eyes and mucous membranes of the respiratory tract, formaldeyde itself limits the concentration human beings can stand. Even very low concentrations are perceived as unpleasant. Irritation thresholds in human beings varies individually. Some data are shown in the following table.

Dose response relationship following human exposure to airborne formal dehyde

EFFECTS	EXPOSURE LEVEL IN PPM
Odor threshold	from 0.05 to 1.0 ppm
Irritation threshold in eyes, nose and throa	from 0.08 to 1.6 ppm
Strong irritation of the upper respiratory tract (cough, lacrimation, extreme disconfort)	from 3.0 to 6.0 ppm
Immediate dyspnea, burning in nose and throat, heavy cough, heavy lacrimation	from10 to 20 ppm
Necrosis of mucous membranes, laryngospasm, pulmonary edema	more than 50 ppm

Symptoms of formaldehyde exposure in man

According to our studies done on humans, pratically all people smell formaldehyde at 1 ppm and for the majority minor irritation effects begin in the range of 1 - 2 ppm. Exposure to as little as 3 ppm is already extremely unpleasant to most people. Symptoms caused by irritation disappear as soon as the formaldehyde exposure ceases. Skin contact with formaldehyde solutions can cause allergic contact dermatitis. However, the percentage of population which may experience an allergic skin reaction to the formaldehyde concentrations is very small having 2 to 4 people out of ten thousand Gaseous formaldehyde does not cause allergies in the respiratory system, on the contrary allergic reactions have been encountered in tabacco smokers and passive smokers deriving from the content of formaldehyde in tabacco.

Skin penetration of formaldehyde is negligible: 0.2% penetrated the skin of man, 0.5% penetrated the skin of monkeys and 5% the skin of rats.

To date it has not yet been demonstrated world wide that formaldehyde can cause cancer in man at the concentrations human beings can be exposured to.

Due to its rapid methabolism in the upper respiratory airways it is highly improbable that formaldehyde may act as a systemic carcinogen. There was no increase in formaldehyde blood levels after inhalation of 1.9 ppm for 40 minutes by volunteers and of about 14 ppm for 2 hours by rats.

GENOTOXYCITY, MUTAGENIC AND TERATOGENIC POTENTIA

Formaldehyde in ZEROG3RM® is weakly genotoxic in vitro in several systems including mammalian cells, however, mostly at high concentration or at toxic levels.

There is no evidence that formaldehyde is mutagenic in mammalian systems «in vivo».

The only indication of an in vivo genotoxic effect is the formation of DNA-protein cross-links in the nasal epithelium of rats, i.e. at the site of impact, after inhalation of 2 to 6 ppm of formaldehyde. There were no DNA-protein cross-links at 0.9 ppm formaldehyde inhalation. DNA-protein cross-links caused by formaldehyde are rapidly repaired. There is no convincing evidence demonstrating mutagenic or teratogenic effects in humans.

Effects of embriotoxicity and fertility on animal reproduction have never been encountered.

TOLERANCE IN ENVIRONMENTAL CONCENTRATION

(CONTROLLED MICROCLIMATE)

In a controlled microclimate such as zoothecnical environment, the maximum admittable concentration of formaldehyde, for an exposition up to 8 hours per day, is about 5 ppm. T.L.V. (THRESHOLD LIMIT VALUES – A.C.G.I.H.): 2 ppm

PHARMACOCINETIC OF ZEROG3RM®

Human blood oxidizes 30% of formaldehyde at formic acid in 4 hours.

Exogenous paraformaldehyde is metabolized by erythrocytes into formic acid with a half-life period of 1 minute. Also in dogs, through oral tract (per os), formaldehyde is rapidly absorbed and oxidized into formic acid.

In rats and mices, per os, the radioactivity is spread all over the body by C 14 already after 5 minutes

Elimination: 40% is breathed out after 12 hours, 10% by urine, 1% by excreta. After 96 hours 10% is left.

Formaldehyde is absorbed by the digestive tract and by inhalation, while skin penetration is negligible What is characteristic of its pharmacocynetic is that formaldehyde isn>t accumulated in human blood after its absorption because it rapidly disappears. Haematic concentration trend of formaldehyde may be seen looking at the haematic rates of Formic Aldehyde after intravenous giving. Studies on monkeys have shown that after giving formaldehyde in dose of 1 mol/Kg for 2-4 minutes, the highest concentration in blood is reached in 5 minutes from the beginning of intravenous giving and that in 10 minutes the formaldehyde cannot be found in blood anymore.

The concentration of formaldehyde in blood isn't measurable because the product is rapidly metabolised into formate and then egested, or converted into carbon dioxide and formic acid or incorporated into other molecules

TOXYCOLOGICAL INFORMATION

In case of contact with skin, wash with water for 15 minutes, possibly take off contaminated dresses and shoes. In case of inhalation, ventilate with fresh air; if it's necessary make mouth to mouth respiration, and only in dangerous conditions (dyspnea) make oxygen-therapy (use breathing apparatus).

CHEMICAL-PHYSICAL INCOMPATIBILITY

Pure paraformaldehyde is chemically incompatible with the following products: liquid oxygen, strong acid, acidic anhydride, strong oxidant and strong reductant agents, brass, cupric, cupric alloys, cupric and silver salts, bronze, isocyanates, tannins, gelatin and bisulfites.

USE AND DOSAGE

According to some autors (Flügge - Medicamenta, Vol. II, page 1519) between 200 and 500 grs of pure formaldehyde is needed for an area of 100 m3 for a period of 4 hours.

One block of ZEROG3RM[®] is able to disinfect an area of 100/400 m3 according to the sector of utilization. Each block of ZEROG3RM[®] must be placed on a metallic tray or on a heat-resistant material. The flame spreads all over the block until it becomes black and then it has to be extinguished by covering it for a few seconds: a slow flameless combustion has begun.

Therefore a constant emission of formaldehyde gas is obtained for about 3 hours and the block is left to fumigate until consumed.



SAFETY RULES IN MANIPOLATION OF ZEROG3RM®

Protect face with a mask that has organic gas filter and eyes with protective glasses before performing

Leave the room after igniting the block and go back in again only after 8 hours. At the end of this period put on individual protective devices and open doors and windows in order to air the place and enter again only when the typical odor of formaldehyde has gone away.

SAFETY RULES IN CASE OF FIRE

In case of fire carbon monoxide and bioxide are generated. To put out the fire use carbon dioxide fire extinguishers.

INDICATIONS

With ZEROG3RM[®] the following aims are achieved:

- 1) strong and lasting bactericide power.
- 2) proved innocuity for most materials.
- 3) rapid and simple application.

For its polyvalence of use against micro-organism and virus and for its simple application, ZEROG3RM® is used in zoothecnical sector to disinfect all kinds of breeding: poultry houses, pig pens, cow sheds, stables, rabbit-breedings and, in agricultural sector it is used to disinfect storagebins.

The ZEROG3RM® is also recommended for disinfection of holds and for all kinds of places that need a specific capillary disinfection.

PACKAGE

The ZEROG3RM® is packed in cartons of 20 blocks 700 grs each (+/- 3%).

Each block is sealed in an envelope on which are printed the instructions for use.



Fumigating Block With Sanitizing Action

OTHER TECHNICAL INFORMATION

Biocide activity of ZEROG3RM®

ZEROG3RM[®] has a strong bactericide power against most pathogenic germs.

Biocide activity has been estimated in fractions of specific time. The tests were made using 1 block of ZEROG3RM® 700 grs. 45 Petri's plates were inoculated by different selectioned microbic stocks with charge values of about 109 UFC/gr.

These inoculated plates were exposed to the fumigant action of 1 block of ZEROG3RM® 700 grs. The tested place was of about 320 m3.

	то	Т5	Т10	T15	Т20
Colibacillus	+ + + + +	+ + +	+	-	-
Salmonellae	+ + + + +	+ + +	-	-	-
Streptococcus	+ + + + +	+ +	-	-	-
Staphilcoccus	+ + + + +	+ + +	+	-	-
Pneumococcus	+ + + + +	+ + + +	+ +	+	-
Brucellae	+ + + + +	+ +	-	-	-
Shigellae	+ + + + +	+ + +	+	-	-
Pasteurellae	+ + + + +	+ + +	+ +	-	-
Proteus	+ + + + +	+ +	+	-	_

Legend: MPN/gr

MPN of survived cells per gr of culture medium

+ + + + +	= c.ca 10 ⁹ MPN	+ +	= c.ca 10 ² MPN
+ + + +	= c.ca 10 ⁷ MPN	+	= T.n.q. Traces not quantificable
+ + +	= c.ca 10 ⁵ MPN	_	= No living cells

The use of ZEROG3RM® in farms

The use of formaldehyde or phormaldehyde is well known to all breeders, who use it all over the world for their thorough disinfections.

It is commonly used in association with potassium permanganate and all breeders are therefore aware that these treatments must be carried out in closed environments, where the presence of animals and people must be avoided. After accurate studies and long experimentations we succeded in producing a product based on paraformaldehyde, producing phormic aldehyde - pure and not toxic - with a higher and lasting disinfecting power and higher activity.

This product is made and sold with the name of ZEROG3RM®. ZEROG3RM® through a slow smoky combustion produces a dry and pure gas, innocuous because it does not contain neither carbonium oxide nor any other toxic substances.

This gas is absolutely anhydrous and therefore lighter than the air: it will spread in a homogeneous way in all places.

Its polymerisation takes place after more than 6 hours of its the application, so its disinfecting power will be active for a period that is long enough to eliminate all dangerous micro-organism.

From what briefly explained above the high efficacy of ZEROG3RM[®] and its practical use are clearly shown.

The use of ZEROG3RM® in hatcheries

According to statements made by O. Siegemann from Germany and E. Hong from England, conditions of reciprocal infections between chicks are so favourable in the hatcheries that many of them can get infected. This is due to the humidity of the environment which is particularly favourable to the multiplication of infective pathogenic agents and germs.

Pathogenic agents can be listed as follows:

Microbs taken before lay: to say Salmonella pullorum, Salmonella gallinarum, many salmonellae, Mycoplasma spp, infectious avian epidemic tremour, leucosis and possibly other virus, probably including infective bronchitis; microbs taken after lay: to say Salmonella typhimurium and other salmonellae, as well as pathogenic strains of Escherichia coli, fungi infections caused by Aspergillu and contaminations from Staphilococcus aureus.

Because of the above mentioned diseases it is imperative that all the cleaning process, with particular reference to disinfection, must be carried out with the utmost care and attention.

It is well known, as stated by Zeetti and Martini, that the Salmonella pullorum is killed by phormaldehyde in 5 to 10 minutes, according to technique used, to the type of hatch used and especially according to the system of ventilation and distribution of gas circulation inside the hatch.

As stated by prof. Caporale, the most effective disinfections in case of newcastle disease are those carried out with phormaldehyde and, as indicated by prof. Secchione of the public hygiene and health ministry, disinfections of environments carried out with phormaline are recommended against staphilococcus aureus, diphteria and tubercolosis.

As stated by J.E. Farok and G.W. Wright, all germs of paratiphum and tiphum are killed within 30 minutes when phormaline is introduced in the environment.

From what stated above it clearly appears that phormaldehyde can be considered as the most effective disinfectant and ZEROG3RM[®], by developing phormaldehyde gas, is the best disinfectant for hatcheries.

The use of ZEROG3RM® in the prophilaxis of respiratory diseases in animals

Main respiratory diseases in animals are: infectious bronchitis, infectious coryza, chronical respiratory

disease (CRD), newcastle disease, infectious laryngo tracheitis, aspergillosis, avian colera, fowl pox Each of these diseases has like pathogenic agent a virus or a fungi (like aspergillus) or a bacteria (like cholera). These agents have different incubation periods and own symptoms.

All of them, on the contrary, have in common the infectious factor. This is the reason why all experts always recommend to associate powerful disinfection for any place to all sulphanomides antibiotics and vaccinating treatments (for animals).

Phormaldehyde is known as the best product against bacteria and its use is recommended in preventive prophilaxis.

Thronging of farms, heavy temperature and humidity changes are normally the main causes for outbreak of respiratory diseases.

The presence of dust, feed residue, feathers in the litters may be also part of the causes for these diseases. Allergies weaken the organism and therefore favour respiratory infections. Parasitic diseases may often favour the outbreak of respiratory symptoms because of the weakening of organism and therefore worms, coccidian and protozoa can have harmful action on health and defences of animals

All experts agree that the air sterilization carried out in the presence of animals is to be considered as a good precaution.

Therefore we are suggesting to use ZEROG3RM® because it develops phormaldehyde gas, particularly in very humid periods and when farms are overcrowded.

It must be kept in mind that respiratory infections can be completely annulled if they are faced at the beginning and a few hours delay can be the cause of negative results.

COMPONENT %			COMPONENT %
Paraformaldehyde	Precursor	CAS N. 30525-89-4	37%
Paraffin solid state	Excipient	CAS N. 92045-76-6	25%
Wood powder	Excipients	CAS N. none	38%

Chemical of Tablet

