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The Return of the Fumigants

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Introduction in form of history

In 1994, Jonathan Banks at the 6th IWCSPP in Canberra made this statement: Fumigation, an endangered technology?

He began his talk with a paper from Bond in1984 who was able to list more than a dozen materials, many of which are in widespread for this purpose. There are various reasons for their disappearance: health (suspected or alleged carcinogens), lack of interest, no food registration, notoriously flammable, etc.

At the beginning of 2005, only two fumigants had some future use: the old phosphine and the new but not yet registered sulfuryl fluoride for stored product protection, Profume®. Methyl bromide was normally phased out on January 1, even if critical uses still allow for some consumption awaiting alternatives, with an exemption for QPS usages (Quarantine and Preshipment)

In March 2005, a new formula of a formerly used fumigant (ethyl formate), Vapormate® was first registered in Australia for stored product protection and some agricultural usages. In the same year, ethanedinitrile was proposed for a registration for wood, in the perspective of the ISPM 15. At least, carbonyl sulphide is proposed for grain fumigation with the clever name of cosmic® and for wood disinfestations, but only for dry wood.

General statements

The need for fumigants

The use of gases has a place in the spectrum of the stored product protection. Disinfestation can be carried out on products in bags, or in bulk without turning the grain and all stages can be killed in a fairly short time.

Contact insecticides work with their residues. Now, at least in the EU, the review of all pesticides has led to the elimination of many compounds, because data are not comprehensive or they show a toxicity that is unacceptable for the current rules. The MRL are going to be lowered and many compounds phased out. They are spread in very thin particles which implies moving the grain. A good homogenization is best performed by spraying the foot of an elevator. In these conditions, the formulation quantity is very low, 4 to 8 litres per 100 tons.

Physical techniques are used globally on a small scale in niches where products are expensive enough to warrant their use: spices, special quality of grain or legumes, etc. These techniques are heat and cold and modified atmospheres.

Consequences of the Methyl bromide (MeBr) phased out

The MeBr phase-out has many consequences,

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some are good, some are bad, but, in all cases, this change has and will cost a lot.

As MeBr was so effective on a very broad spectrum of pests and so cheap, recognized all over the world as such, it has inhibited a lot of research. The parties of the Montreal Protocol were surprised to find that alternatives is so difficult. The research really began after its inclusion in the ozone depletion substances in 1992.

Nevertheless, for stored products, only one fumigant can replace MeBr, phosphine. That leads to misuses of this compound since the exposure time is very long and relative humidity and temperature play a big role in the efficacy. This may lead to insect resistance. This risky situation has pushed the research towards lots of new compounds.

The tendency is now to use the fumigants safely

When a toxic gas is recognized as a good tool against insects, the risks must be very carefully documented. Risks at the time of the fumigation for fumigation staff, for the workers not implicated in the fumigation and the public.

The risks for the fumigators and other workers are defined by long- and short-term occupational exposure limits, or other standards according to the countries. In the European Union, it has become almost impossible to register a gas which cannot be measured at these low levels for the fumigators-but they can wear respiratory protection- and more for other workers, particularly to give the clearance to enter the premises.

There are two ways to use a fumigant safely:

Forbid any person in any part of the warehouse during any fumigation inside, no matter what size-that is the case in the USA-or define an area large enough to be sure that gas concentrations are far below the limits.

Allow people to work close to the fumigation area, but the fumigator in charge has to design a protocol to allow gas concentration measurements any time and foresee the actions to be taken.

Many new kinds of meters are now very effective, small and sometimes cheap, though not always.

Current status of the fumigants

Phosphine

Phosphine is currently the only fumigant that is registered worldwide for the disinfestation of durable commodities. The phase-out of methyl bromide has drastically increased its use not in quantity, but in the variety of stored products fumigated like spices, cocoa beans, dried fruit, nuts and even now fresh fruit like table grapes, kiwi, etc (Horn et al., 2005).

The main changes in the current and future uses of phosphine come from the diversity of the sources of phosphine which can now be produced in different ways.

The traditional way to obtain phosphine is the reaction between the solid formulation of aluminium or magnesium phosphide and the ambient humidity.

It is an efficient way if the right conditions are present. The relationship between reaction time and the relative humidity may cause some problems. The data gives an idea of the influence of relative humidity: the ed doubles between 9.7 g/m^3 of water in air and 25 g/m^3. In dry conditions, the release is so slow that exposure time should be increased to take into account the length of hydrolysis, for example, instead of 4 days at 30 °C for Lepidoptera, we should use 8 days.

The problem is easily overcome if gas measurements are performed daily. It is then easy to see the concentration slowly but continuously increasing and the exposure time lengthening. If the exposure time is not increased, the concentrations will be too low and then the fumigation will fail, the powder remaining after the fumigation will still contain a large proportion of phosphide which will explode if put in water.

The powder which remains after the reaction has taken place even after deactivation by water still contains phosphide. For small quantities, the material is buried, but it is not possible when large quantities are produced regularly and it is then necessary to resort to a waste company.

Cylinder-based formulations containing phosphine mixed with carbon dioxide, with nitrogen, or even just pure have been developed in recent years for use as fumigants. These formulations allow a quick gas release and concentrations build up very quickly. With a solid formulation, it is necessary to introduce all at once a quantity which takes into account sorption and leaks. With cylinder-based formulations, the dosage can be adjusted from time to time to be above the minimum concentration and the total quantity delivered is then lowered.

The purity of phosphine is a big advantage for sensitive products like nuts or fresh fruits. It proves to be a real advantage.

Phosphine may also be produced very quickly and independently of weather conditions with generators using special solid phosphide formulation which can be put into water without exploding. Phosphine is produced almost as quickly as with cylinder-based formulations, without the need to transport the cylinders. Nevertheless, they leave slurry and furthermore, the phosphine contains some ammonia and is then not usable for fresh fruits or other sensitive products.

One argument given by the producers of quick phosphine release is a much shorter exposure time. This is true in dry conditions where hydrolysis is very slow, but in all other cases, only several hours are saved. The reason is the phosphine's complex way of working (Ducom, 2005). Phosphine acts on two main enzymes, oxydase cytochrome and catalase. These two enzymes regulate the conditioning of oxygen to enter the mitochondrion. Blocking their action makes it impossible for oxygen to penetrate into the cell leading to the formation of super oxides which are the true biocidal agents. The mainspring of this system is iron, the change from ferrous iron to ferric iron ($Fe^{++} \rightarrow Fe^{+++}$). The deactivation of the enzymes occurs at low phosphine concentrations, but it proceeds according to the acquisition of resistance. For example, in Australia, the minimal concentration to block the enzymes went, for all species, from 25 ppm in 1990 to more than 100 ppm in 2004. In many countries, 200 ppm has been chosen, like in France, the UK or Australia.

Then, the time gained from solid formulation and quick phosphine release will be the time for the solid preparation to give 100 or 200 ppm. This time is very short, several hours in "normal" conditions.

Resistance to phosphine is a great concern and it can be overcome by using meters every day during gas exposure to be sure that the concentration is always above the minimum required.

Exposure time is always a matter of discussion between some producers and the advisors: For example, at 30 °C, most of the labels recommend, for any insect, 3 days while scientists and technicians recommend for this temperature between 4 days for all insects, except the *Sitophilus* spp for whom 5 to 15 days are required.

In conclusion, there is no "return" of phosphine, but a great choice to produce or use phosphine in many different ways for different technical needs and prices.

Ethyl Formate (EF)

Ethyl Formate, not alone, but as a mixture with some other compounds or in a vacuum, may be the most promising fumigant for grains and all other stored and fresh products.

It is known to break down into naturally-occurring products - formic acid and ethanol. Ethyl formate occurs naturally in soil, water, vegetation and a range of raw and processed foods (from 0.05 to 1 mg/kg).

EF is currently registered in Australia for the disinfestation of dried fruit and is particularly used for sultanas where it is added as a liquid to packages of fruit before they are sealed.

It is a liquid at room temperature, its toxicity was reviewed by Muthu et al. (1984). It kills rapidly, in several hours, and it was re-evaluated by the Stored Grain Laboratory in Australia to use on stored product insects. EF is a GRAS (Generally Recognized As Safe) food additive.

To overcome its flammability for commercial use on a large scale, research was oriented around the mixing of EF with synergist to reduce the dose and flammability.

EF is mixed with liquid carbon dioxide in the proportion of 16.7 wt % ethyl formate, equivalent to 11 volume % in gaseous CO2 when vaporised missing (Ryan and Bishop, 2003). It is produced by BOC under the trade name, VAPORMATE®, registered in Australia since 22 March 2005 (Australian Pesticide & Veterinary Medicines Authority, APVMA Reference #56186). It is a new cereal grain, stored product and fresh produce fumigant for application by pressurised cylinders. CO2 acts in two ways: the mixture in this proportion is non-flammable and it has an synergized effect. It is a rapid-acting fumigant, effective in a range of from 4 to 24 hours. It is a safe fumigant since the TLV is 100 ppm for EF and 5,000 ppm for CO2.

The rapid breakdown of VAPORMATE® ensures that there are no issues with residual chemicals on treated goods, metabolism giving hydrolysis products, ethanol and formic acid. There are no withholding periods after treatment (Ren and Desmarchelier, 2001; Vu and Ren, 2004).

VAPORMATE® was first registered for grain and oilseeds with a dosage only for adults at 420 g/m^3 in 24 h. New experiments were performed to allow for new dosages with complete kill of all stages of all insects 660 g/m^3 held for 4hours or 420 g/m^3 held for 24 hours, but for Rice weevils (*Sitophilus oryzae*): 940 g/m^3 held for 72 hours. Preliminary Germination trials on malt barley treatment at 5 times the label rate show no significant difference in germination energy (Haritos, 2006).

This shows that we are at the beginning of a new technique and many adjustment are to be made. In addition, the research was carried out in Australia where the temperature, grain quality, insect species, etc. is not exactly the same as in other parts of the world. For example, in countries like France or Germany, grains on average have a 14 % moisture content, temperature from 15 to 20 °C and the most common insect species are *Oryzaephilus surinnamensis* or *Sitophilus granarius*.

A lot of work has to be done to define the right application conditions.

VAPORMATE® is also registered for grain storage premises and equipment at an application rate of 420 g/m” for 6 hours.

In other fields like dried fruit and nuts, semi-dried fruit like fresh chestnuts and dates, this compound has many “a priori” advantages like a quick exposure time, no quality deterioration for the product, safe use, no residues, etc.

The mode of action seems to be the inhibition of Cytochrome C Oxidase by the formic acid resulting of the hydrolysis of EF (Haritos and Dojchinov, 2003).

SGRL is also investigating ethyl formate synergized with an isothiocyanic ester like methyl or allyl isothiocyanate in a slow-release formulation to enable the compound to be directly applied to grain like a contact insecticide. In these conditions, gastightness is not as important as with conventional fumigants because sorption takes place at a very high level, but as the material is well homogenised, most of the gas has penetrated into the kernel.

EF may be also be used in a vacuum which increases the efficacy like for methyl bromide (Siwei Liu et al., 2004) This is a very interesting field of research for quick fumigations and uses the present vacuum chambers which exist in many countries.

Sulfuryl fluoride (SF)

Sulfuryl fluoride now has been widely approved for use in flour mills and empty food processing facilities since the first approval in Switzerland in 2003. Registrations are increasing for use on grains, beans, dried fruit and tree nuts. Potentially, it could also be used for many other products like beverages, legumes, some niches like fresh chestnuts and dates and for wood packaging as a quarantine fumigation. It is toxic to post-embryonic stages of insects, but the eggs of many moths and beetles are very tolerant, especially at lower temperatures. Early research indicated that the lower efficacy on eggs is primarily due to slow penetration through the chorion and eggshell missing.

Its current main use is for flour mills, but its adoption as an alternative to methyl bromide has been very slow for economic reasons linked to the difficulty to kill eggs, especially those of *Tribolium castaneum* which require a high CTP and a high temperature. In comparison, the CTP for the same temperature is 5 to 10 times higher for SF than for MeBr. As a result, it is very important to enhance sealing techniques for gas confinement and to follow the concentrations throughout the exposure time.

A way to decrease the cost is to kill only the postembryonic stages; which allows one to cut the CTP almost in half. It is a controversial technique which leaves a part of egg stages of the populations alive. The question is if the population rebound is significantly higher with this stock of eggs. Is the reinfestation by the neighboring external population much higher than that coming from the eggs themselves?

For stored product fumigation, it is much easier to reach the right CTP as gastightness is under control in a chamber or under tarpaulin. Nevertheless, food tolerances have to be established for residues in sulfuryl fluoride and fluorides in the products.

Carbonyl sulfide (COS)

Carbonyl sulfide is a potential fumigant for stored products able to replace methyl bromide or phosphine in many situations. It is a gas at room temperature. A lot of work has been done on it at the SGRL, CSIRO, Australia.

Laboratory studies have shown that COS is effective on a wide range of stored-product pests in all stages, including mites, at concentrations from 10 to 40 g/m^3, at exposure times of 1 to 5 days at temperature $\geq$ 5 °C (Desmarchelier, 1994). It is important to note that this gas is equitoxic at most temperatures down to the lowest tested temperature of 5 °C. *Sitophilus oryzae* is the most naturally tolerant and studies at CSIRO provided a range of exposure time/ concentration regimes to give disinfestation level mortalities, for example concentrations of 20 g/ m^3 for an exposure time of 5 days is a particularly good combination, (Weller and Morton, 2001).

There is no adverse effect on the quality of bread, noodles, the malting and brewing characteristics of barley, nor a significant effect on germination or plumule length (Wright, 2003)

COS should be applied with a recirculation system even if it penetrates grain and timber more easily than does methyl bromide (Desmarchellier, 1998).

COS has been trademarked in Australia as COSMIC™. BOC has an agreement with CSIRO for the manufacture and worldwide distribution. This company made a COS pesticide registration application to Australian Pesticide & Veterinary Medicines Authority [APVMA] on 24 June 2005. This on-going APVMA approval process will takes ~ 2 years.

EthaneDiNitrile (EDN)

Ethane dinitrile is one of the name of CN-CN, better known as cyanogen. It has the wider spectrum of efficacy among the new fumigants since it can be used for treating soil, insect pests, weeds and diseases. It is an environmentally-safe fumigant, a colourless gas with an almond-like odor. It is a gas at room temperature(boiling point –21.2 °C) and it is soluble in water. The threshold limit value (TLV) of 10 ppm (v/v) compares favourably with that of both methyl bromide (5 ppm) and phosphine (0.3 ppm). EDN's main route of decomposition is to derivatives of oxalic acid. It is much more toxic than methyl bromide and kills very quickly, except for *Sitophilus* spp egg stages where 5 days are required to achieve complete mortality (Hooper et al., 2003).

As it is phototoxic and poorly efficient on *Sitophilus* spp, it is not a future grain fumigant. It is a potential mill fumigant. It is very interesting for timber, artifacts, soil fumigation and for the medical industry. Relative humidity is a very important factor of efficacy, it cannot work in dry conditions.

CSIRO and BOC have agreed to commercialize ethanedinitrile (EDN). BOC made an EDN pesticide registration application to Australian Pesticide & Veterinary Medicines Authority [APVMA] on 24 June 2005. This on-going APVMA approval process will takes ~ 2 years.

Conclusion

The return of the fumigant is a reality. At this writing, phosphine is no longer the only available fumigant. There are already two fumigants for post harvest disinfestation registered since the last conference in York in 2002, sulfuryl fluoride (PROFUME™) in 2003 in Switzerland and a mixture of ethyl formate in liquid carbon dioxide(VAPORMATE®). There is a wide choice to produce or use phosphine in many different ways suitable for different technical needs and prices: solid formulations with relative humidity, cylinder-based formulations with or without CO2 or generators producing phosphine by pouring a granular form of aluminium or magnesium phosphide in water. Nevertheless, the exposure time is still long whatever the production technique. Ethyl formate used mixed with different compounds, mainly CO2 under the trade name of VAPORMATE®, kills insects rapidly, in several hours. It is safe for the users and does not leave any residue. Nevertheless, its efficacy on sitophilus oryzae eggs needs more time and a higher dosage than all other insect species. This mixture could be used on almost all products, but a lot of research is needed to attain precise efficacy conditions.

Carbonyl sulphide is a potential fumigant for grain and some other stored products, but its use seems more difficult/complicated than other ones. Ethanedinitrile has a great future, but except for structural fumigation its future is for quarantine , artifacts and soil fumigations.

All the fumigants have a weak point: the egg stage of many species of insects, with a particularly large tolerance for *Sitophilus* spp. The future new fumigant will the one able to challenge this almost universal weakness of current fumigants.

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