Autoclaving of aqueous solutions in sealed containers: feasibility and risks

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ABSTRACT: *This article is intended as a basic introduction on feasibility and risks of autoclaving aqueous solutions in sealed containers. Another article, Aqueous solutions in sealed containers: internal pressure under autoclaving, provides a technical approach to the matter. The feasibility and the level of risk of autoclaving sealed containers of liquid solutions under pure saturated steam conditions (e.g. in "classical" steam autoclaves, without "counterpressure") depends on a large amount of factors. The knowledge of the mechanical resistance of the material, of which the containers are made, is very important to ascertain whether the differential pressure shall be compensated for (and to which extent), or may not be compensated for.*

KEYWORDS: moist-heat sterilization, steam sterilization of aqueous solutions, sealed containers, headspace volume, internal pressure, autoclaving, autoclave, superheated water sterilizers, steam/ air mixture sterilizers

Regardless to how much containers are stressed during autoclaving, a point of an utmost importance is that **containers must finally be unloaded from the autoclave into the ambient, where no counterpressure is applicable at all.** Thus, the unloading temperature is by far the most important factor to reduce the risk of fatal accidents for the operators. Both the probability of explosion of the load outside the autoclave, and the very harmful effect of the hot solutions on the human body become much smaller if the unloading temperature is reduced from 100 °C (very high risk) to:

- 80 °C (acceptable risk for small containers with filling levels lower than 80 %)
- 65 °C (acceptable risk for containers with filling levels lower than 90 %).

Filling levels higher than 90 % must always be avoided, but in the case the containers are sealed by a movable plug and enough space is granted for the displacement of the plug during autoclaving *without protruding it outside of the syringe tube* (this is the typical case of pre-filled syringes).

In addition to the risk of explosion during autoclaving, and to the much bigger risk of explosion during unloading operations, another risk shall be considered. If the differential pressure is not compensated, containers sealed with stoppers might lose part of their content during autoclaving, due to the sealing being not perfectly tight, or becoming not perfectly tight at sterilization temperature. These losses would cause the containers going under vacuum during the cooling, so that they might subsequently, i.e. during their shelf-life, suck non-sterile air from the ambient. This is a major reason why LVP containers are usually sterilized under counterpressure, but does apply only to containers that are sealed with stoppers.

All the above considerations, and the more detailed facts summarized in the files quoted above, have determined the most serious autoclave Manufacturers. to warn Customers and End Users, not to use pure saturated steam autoclaves for the sterilization of containers of aqueous solutions of bigger volume than 100 or 150 ml: the actually applicable limit depends on the mechanical resistance of the containers. However, even if counterpressure autoclaves are used (either superheated water autoclaves or steam & air ones), **the risk of accidents while unloading the autoclave may be reduced to an acceptable level only by a conscious and sound selection of the unloading temperature**.

To summarize:

Counterpressure autoclaves do practically eliminate the risks of:

a) explosion of containers during autoclaving: this risk is higher with very large ampoules and with containers made by thinner of weaker glass;

b) suction of non-sterile ambient air after the cooling into containers *sealed by stoppers*: this risk does not apply to ampoules, regardless to their volume.
c) and allow for coping with the risk of misshaping or damaging plastic container, the material of which quickly loses mechanical strength at higher temperature, this of the resulting in permanent deformation of them, not acceptable from the commercial point of view.

On the contrary, both risks have to be considered when pure saturated steam autoclaves are used for sterilizing solutions in sealed containers: counterpressure autoclaves are definitely safer for the industrial yield and for the final quality of the product. The choice between the two types of counterpressure autoclaves (superheated water or steam & air) will depend on other factors, mainly the possible demand for final drying inside the autoclave and the material of the containers.

Neither counterpressure, nor saturated steam autoclaves can deal with the risk of explosion of containers *outside the autoclaves*, **but by providing a safe and reliable method of cooling the autoclave load**. The risk of explosion of the load during and/or after the unloading operations of sterilized loads may obviously result in the loss of the load, but is almost the only cause of major and sometimes deadly accidents connected with moist-heat sterilization.

The risk of explosion of the load outside the autoclave may be reduced to an acceptable level only by a conscious and suitable **choice and respect of the cooling and unloading temperature**. Most modern autoclaves does not allow to step over cooling phases, and provide the possibility of locking doors if a safe temperature has not been reached inside the autoclave chamber. However, the effectiveness of these safety provisions depends on the management policy of end-users, on the knowledge they have about the process and on the extent to which they intend to apply it: a wrong selection of the sterilization program and/or its parameters could frustrate any safety provision by the autoclave manufacturer.

Vacuum after sterilization, sometimes used for challenging the tightness of ampoules, **should be avoided for any case with larger containers. Solutions in solvents other than water, liquid dispersions and emulsions usually generate internal pressures dramatically higher than in the case of water solutions, and the risk of flammability may often occur. For these reasons, any liquid different from aqueous solutions must not be processed under heat, but in the case that a special and expressly designed autoclave is available.**