## **TransAtlantic**Safety

## NON-THRESHOLD TOXICITY MECHANISM

Carcinogenicity (genotoxicity) is conventionally treated as a "non-threshold phenomenon". This means that any exposure, no matter how small, is regarded as conferring some degree of risk in terms of eliciting a genotoxic change. The idea is that any molecule of the genotoxic agent could produce one crucial change in the DNA programme, thus catalysing a series of catastrophic changes, e.g. cancer development.

In reality, there are physiological defence mechanisms that can "detoxify" molecules of genotoxicants before they can attack DNA, and there are also DNA repair mechanisms that can restore back to normal sites of DNA damage. These observations suggest that there may be practical dose thresholds for genotoxicity to be expressed.

However, limitations in the sensitivity of the test methods available mean that it is not possible to determine reliable dose thresholds for the development of genotoxic effects.

The regulatory response to identified genotoxicants is to treat them in a manner commensurate with no reliable threshold dose for the effect being identifiable. Therefore, COSHH 2002 Regulations dictate to reduce all exposures to carcinogens to as low level as reasonably practicable (ALARP) and not just below the WEL.

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## **TOXICITY MECHANISMS**

