# The Crystalline Silica Conundrum

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# Regulatory Updates for Crystalline Silica and Potential Business Implications

- Background on Crystalline Silica Toxicity and Exposure Pathways
- Methods used to generate Hazard Classification data
  - Modified Exposure Methods (NIOSH 7500, AS 2985)
  - Size Weighted Relative Fine Fraction (SWeRF)
- Issues surrounding Hazard Classification under the Globally Harmonized System for Classification and Labeling




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# Crystalline Silica Toxicity

- Crystalline silica (CS) consists of several naturally occurring minerals, including quartz, cristabolite and tridymite.
- Under most conditions CS it is not hazardous, only Respirable Crystalline Silica (RCS) poses a health risk
- Main Health effects of RCS: Silicosis and Lung Cancer
- Less common effects: Chronic Obstructive Pulmonary Disease; Chronic Renal Diseases; Autoimmune disorders




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# Inhalation Exposure Pathway

**Inhalable Particles**

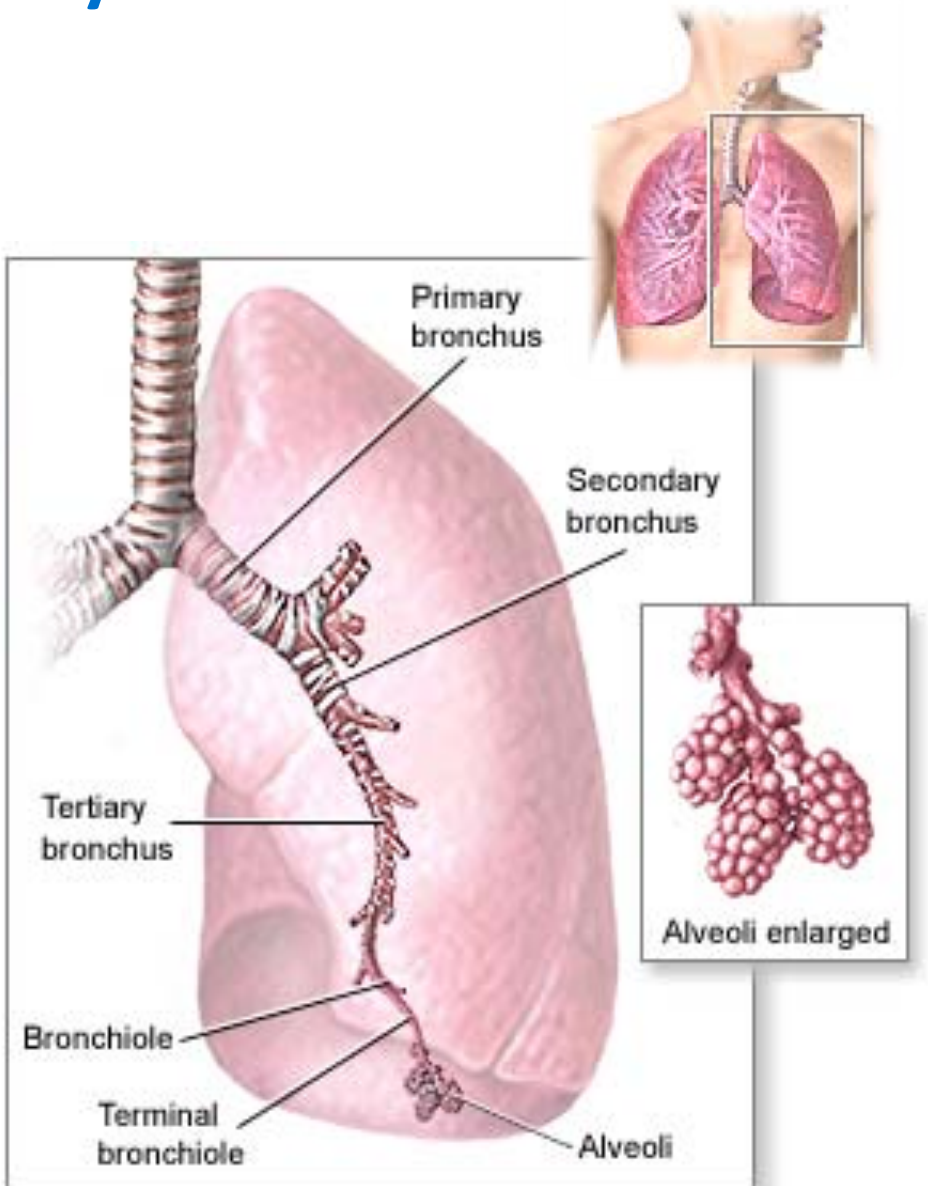
- Particles that can be inhaled into the mouth and nasal cavity
- AD ~100 um

**Thoracic Particles**

- Particles capable of penetrating beyond the larynx into the bronchus
- AD ~10 um

**Respirable Particles**

- Particle capable of entering the uncilliated portions of the lung and being deposited in the alveoli
- AD ~5 um



# Silicosis

It is an irreversible, progressive, disabling and sometimes fatal lung disease

Mechanism: The lung burden of RCS overwhelms the Alveolar Macrophage ability to clear the lung, this induces inflammation and fibrosis in the lung

Types of Silicosis

- Chronic Silicosis: >10 years exposure to low concentrations of RCS; develops 10-30 years after first exposure
- Accelerated Silicosis : develops 5-10 years after exposure to higher concentrations of RCS
- Acute Silicosis: develops a few weeks to 5 years after exposures to high concentrations of RCS

- Relationship of Silicosis and RCS exposure has long been accepted in the medical and scientific community

# Lung Cancer

RCS has been classified as a known human carcinogen (IARC, 2012; OSHA, 2013; NTP, 2011 )

Several Mechanisms for Carcinogenesis have been proposed

1. Direct Genotoxicity (RCS particles are taken up by lung cells and damage DNA)
2. Generation of Reactive Species (RCS Particles produce free radicals that enter cells and damage DNA)
3. Secondary Inflammation-driven Genotoxic Response (RCS particles cause inflammation [silicosis] with generation of reactive species, overwhelming of the antioxidant defense mechanisms in the lung, and leading to tissue injury, repair, and hyperplasia)

Recent authoritative reports (IARC, 2012; OSHA, 2013; NTP, 2011; Environment Canada and Health Canada, 2013) and published review papers (Borm *et al*., 2011; Cox, 2011) provide strong support for a secondary inflammation-driven genotoxic mechanism for RCS caused lung cancer

This mechanism is a threshold response

# CS Classification and Labeling under GHS and EU CLP

Main Decision Points

1. What form of Crystalline Silica to classify, RCS vs. TCS
2. How to measure crystalline silica in a bulk sample
3. Define Classification for Specific Target Organ Toxicity for Repeated Exposures (STOT RE)
4. Define Classification for Carcinogenicity

# RCS vs. TCS for classification

- Hazard classification should be based on the “intrinsic properties of the substance” including hazards "relate[d] to the form or physical state(s) in which the substance or mixture is placed on the market " (CLP Articles 5, 6, and 8.6)
- Most countries and agencies that list CS as a carcinogen specify RCS: Denmark, Sweden, Netherlands, IARC, NTP, OSHA Eurosil, IMA-Europe, etc.
- Industry groups also specify RCS as the relevant species for classification: Eurosil, IMA-Europe, etc

## Advantages:

- More biologically relevant
- Targeted approach for worker protection
- RCS < TCS

## Limitations:

- No agency-approved method for measuring RCS in bulk products
- Some jurisdictions may not accept RCS data
- Costs for testing

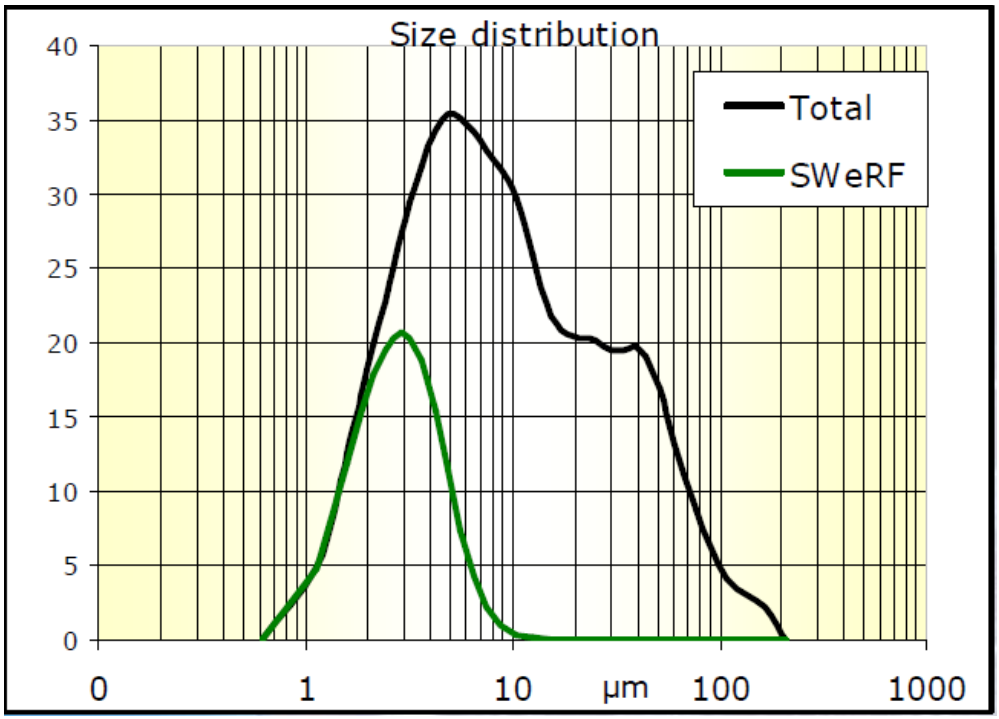
# Respirable Crystalline Silica measurement in bulk samples

- Current validated methods for RCS measurement are for occupational exposure
- Size-fractionated samples of work place atmospheres are collected with small cyclonic pumps
- Exposure samples are problematic for Hazard Assessment
  - Can require long sampling times
  - Difficult to analyze single substances
  - May not be accepted by agencies
- Commercially Available Methods for RCS in Bulk Samples
  - Size Weighted Relevant Fine Fraction (SWeRF) developed by the European Industrial Minerals Association (IMA-Europe)
  - Modified NIOSH 7500
- Other potential methods:  hydrocylcone or dust chamber methods, bulk sample suspension with respirable size fraction sampling

# SWeRF-Size Weighted Relative Fine Fraction

- Combines particle size distribution (PSD) of CS in bulk material with probability factors for alveolar deposition from EN standard 481

| Aerodynamic Diameter (um) | Probability of Deposition (%) |
|---|---|
| 1 | 97.1 |
| 5 | 30 |
| 10 | 1.3 |
| 16 | 0 |




- The $SWeRF_{CS}$ (RCS) is calculated by multiplying the SWeRF of a sample by the TCS of the sample

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# SWeRF-Size Weighted Relative Fine Fraction

- Calculation
  - Sum of the Particle Size Distribution, EN 481 probability, and TCS concentration
  - Assumes all particles have the same density or all materials have same particle size distribution

  Link to SWeRF Calculation Spreadsheet
- Measurement
  - The bulk sample is suspended in a suitable liquid
  - The sedimentation time is calculated for larger particles to settle out of the upper layer of the column.
  - After the calculated time, the supernatant and the fine fraction is removed, filtered, and the filter analyzed for CS concentration by XRD

  Link to Draft Standard

# SWeRF-Size Weighted Relative Fine Fraction

## Advantages:

- Submitted to the European Committee for Standardization (CEN)
- Extensive validation testing (Pensis et a., 2014)
- Strong industry support
- Some countries seem prepared to accept SWeRF data (Germany, Netherlands)

## Limitations:

- CEN expected decision in 2-3 years
- Calculation assumes CS particle size distribution same as bulk sample
- Sedimentation can be problematic technique
- Relies on probability of a particle depositing the alveoli (exposure)
- Some jurisdictions (UK) may not accept SWeRF




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# Modified NIOSH 7500

- Replaces exposure sampling with method to measure PSD of the silicate fraction of the sample
  - Sample Preparation: Ashing to remove excess carbon, Disaggregation, Sonication, etc.
  - TCS measured in sample by XRD
  - Sample is suspended in acetone and deposited on a filter for computer-controlled scanning electron microscopy with energy dispersive spectroscopy (CCSEM-EDS). Determines the size and composition of ~1,000 particles.
  - Mass of the <5 um silica-rich particles x TCS wt %=RCS wt%

# Modified NIOSH 7500

## Advantages:

- More conservative/protective than SWeRF
- Does not assume CS PSD is the same as the bulk PSD
- Does not rely on probability function
- The Laboratory attests that their results are accepted by NIOSH and MSHA (we have not been able to independently verify this claim)

## Limitations:

- Modification has not been approved by regulators
- Estimation, rather than a measurement
- Assumes all Si-rich particles are crystalline
- Sample prep may reduce PSD

# Other Potential RCS Methods

- Australia CSIRO: Bahco Separation with Siroquant XRD
- UK MDHS 101 (2005) Dust cloud generator with cyclone samplers and XRD or FTIR analysis of standards

# Hazard Classification Regulations Updated to Align with Globally Harmonized System (GHS) for Classification and Labeling Chemicals (UN)

**US:** Has adopted the GHS as the new hazard communication standard (HazComm, 2012)

Phase in period for Compliance:

**June 1, 2015 to December 15, 2015**

**EU:** Classification, labelling and packaging of substances and mixture (CLP) aligns EU regulations with GHS

Deadline for Compliance:

**June 1, 2015**




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# Hazard classification of Respirable Crystalline Silica

- General agreement on hazard classification for Specific Target Organ Toxicity Repeat Exposure to the lung via inhalation.

**STOT RE 1**

- There is no globally harmonized carcinogenicity classification for RCS
  - Classification guidance vary by jurisdiction
  - Classifications decisions range from:

**No Classification**

**Carcinogen Category 1A**




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# No Classification for Carcinogenicity

- IMA-Europe, Eurosil, Norway and others have taken the position that
  - Silicosis is a precursor to lung cancer
  - Minimizing the silicosis risk will also minimize the lung cancer risk
  - Thus classification for carcinogenicity is not required (Morfield, 2010)
- Aligns with the EU's Scientific Committee on Occupational Exposure Limits (SCOEL) main conclusions:

> *The main effect in humans of the inhalation of respirable silica dust is silicosis. There is sufficient information to conclude that the relative lung cancer risk is increased in persons with silicosis (and, apparently, not in employees without silicosis exposed to silica dust in quarries and in the ceramic industry). Therefore preventing the onset of silicosis will also reduce the cancer risk. Since a clear threshold for silicosis development cannot be identified, any reduction of exposure will reduce the risk of silicosis.*

# Classification for Carcinogenicity where RCS is a listed carcinogen

- Canada WHMIS classifies RCS as an IARC Group 1
- The Netherlands lists RCS as a Carcinogen Category 1A
- New Zealand lists RCS as a "known or presumed carcinogen to Humans" IARC Group 1
- Germany does not list RCS as a carcinogenic substance, but the AGS did determine that it was a human carcinogen and operations with RCS were included in 2005 TRGS 906 "Catalogue of carcinogenic operations and procedures"
- Denmark and Sweden list RCS as a carcinogen but do not specify the classification

# Carcinogenicity Classification in Jurisdictions which allow self classification

GHS: carcinogenicity categories are clear analogous to IARC Groups

| GHS | IARC | Phrase |
|---|---|---|
| Category 1 A | Group 1 | known human carcinogen |
| Category 1B | Group 2A | probable human carcinogen |
| Category 2 | Group 2B | suspected human carcinogen |

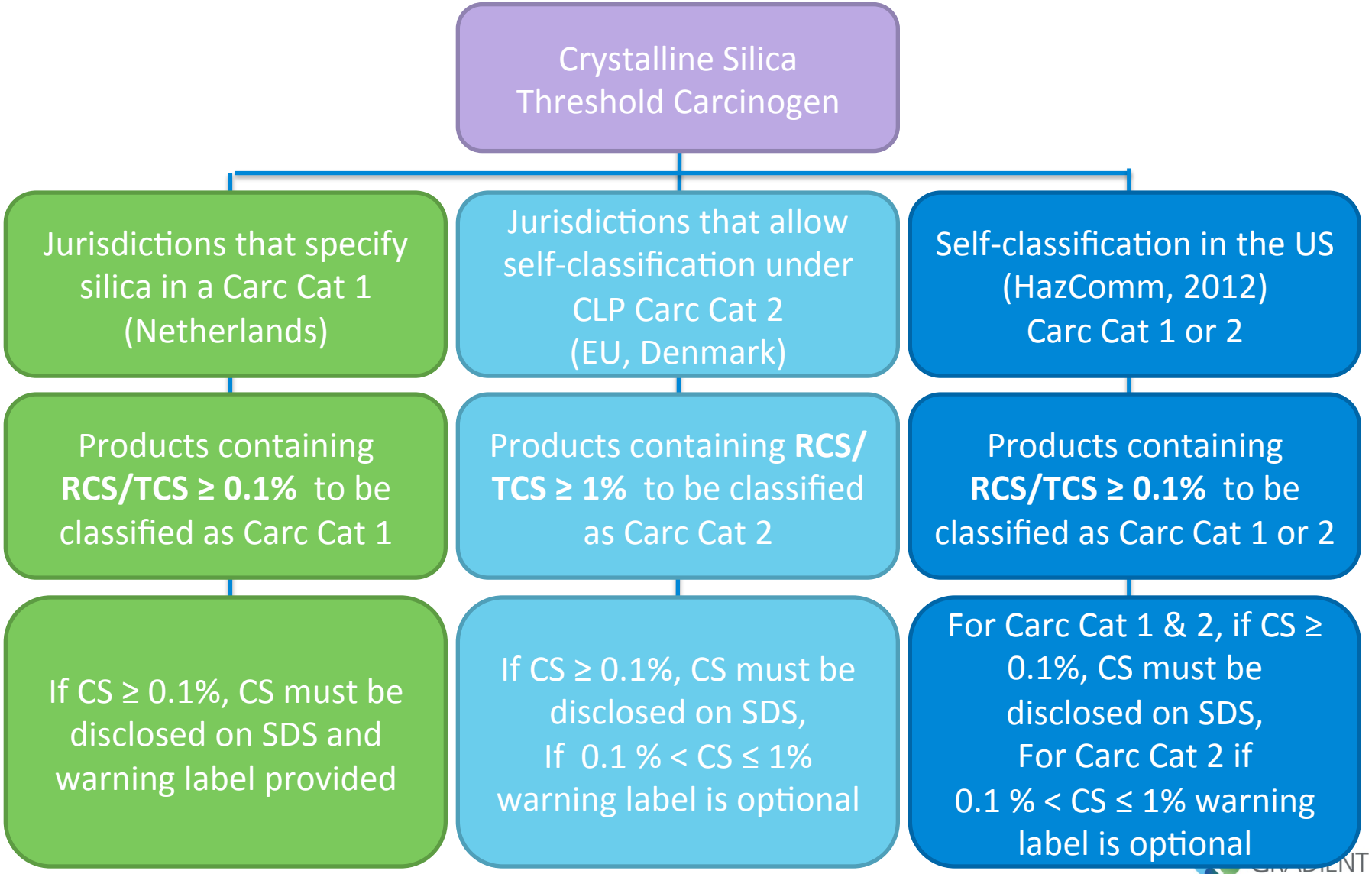
US: HazComm specifically recommends NTP (known human carcinogen) and IARC (Group 1) as sources for classification guidance **though independent evaluation is allowed**

EU: ECHA CLP guidance states that

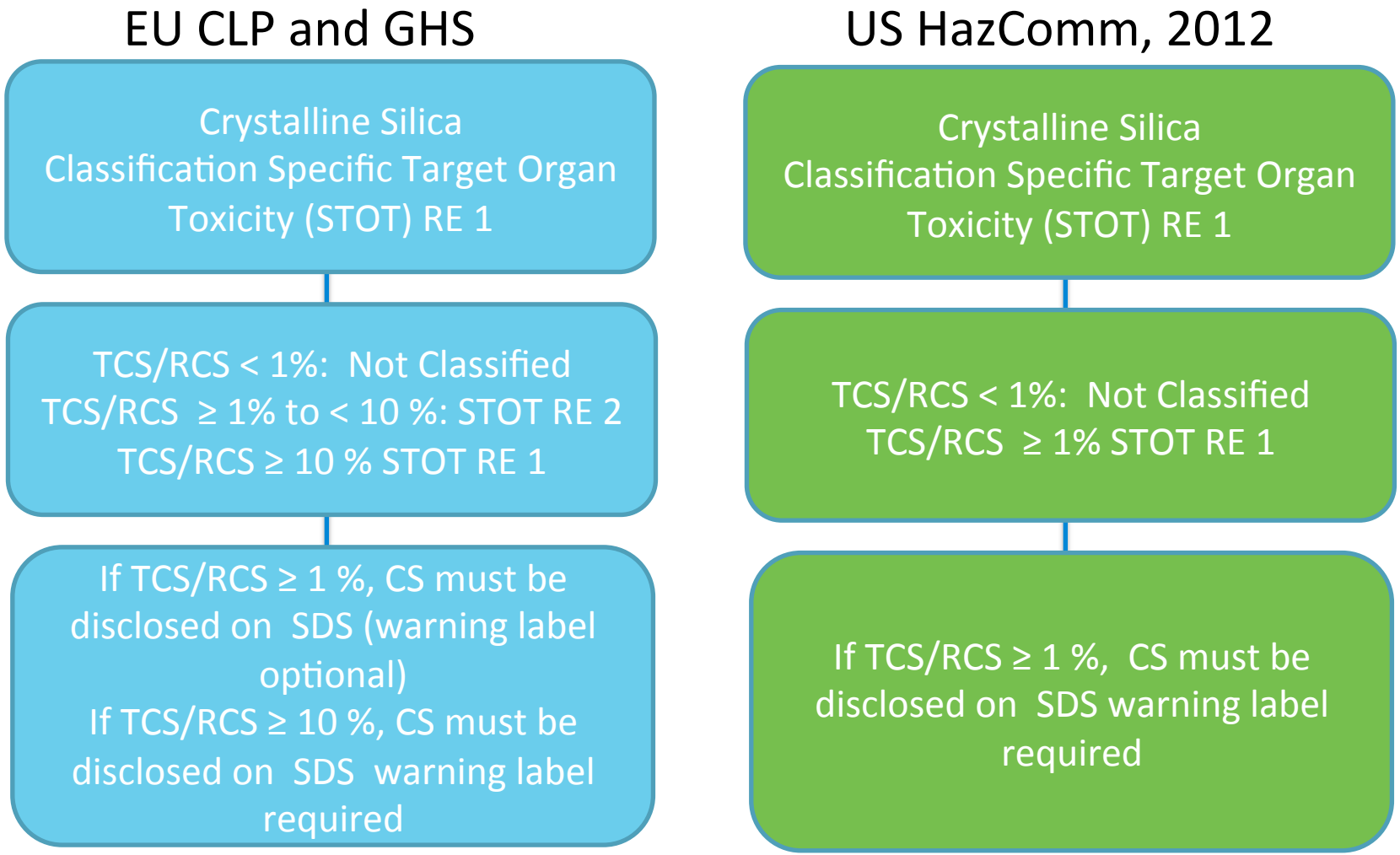
> *In addition, the existence of a secondary mechanism of action with the implication of a practical threshold above a certain dose level (e.g., hormonal effects on target organs or on mechanisms of physiological regulation, chronic stimulation of cell proliferation) may lead to a downgrading of a Category 1 to Category 2 classification.* (ECHA, 2013, p. 401)

Thus, in the EU, RCS can be classified as a Carcinogen Category 2

# Implication for Carcinogenicity Classification of Mixtures under CLP and GHS



# Classification of Mixtures for Specific Target Organ Toxicity-Repeated Exposure (STOT RE)



# Implications

- Companies who are more  conservative/protective in their classification may be at a disadvantage to competitors who choose less conservative classifications
- Classification of a product containing RCS as a carcinogen in one country, but not another, may be a legal liability
- Producing and managing jurisdiction specific SDSs can be operationally challenging