

***Cesare Maltoni Cancer Research Center (CMCRC)
Ramazzini Institute (RI), Bologna Italy***



CHE Partnership call:

**Glyphosate:
The Increasing Use of
GBHs Worldwide and
Implications for Human
Health**

Thursday, April 28th 2016

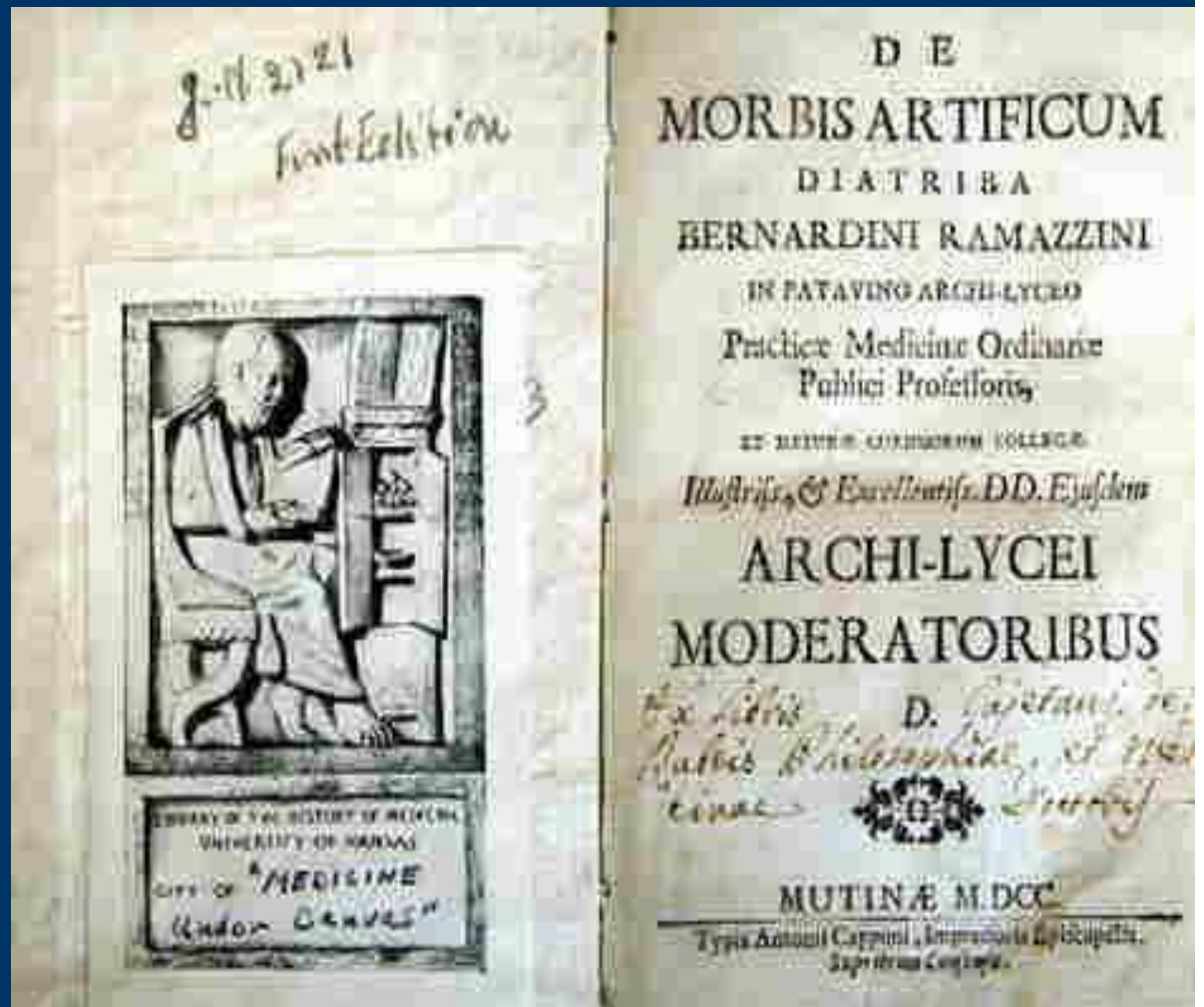
Dr. Fiorella Belpoggi
Director

Research Department
Ramazzini Institute

Bernardino Ramazzini



Carpi, 1633 – Padua, 1714



De morbis artificum diatriba, (1700)

Ramazzini Institute

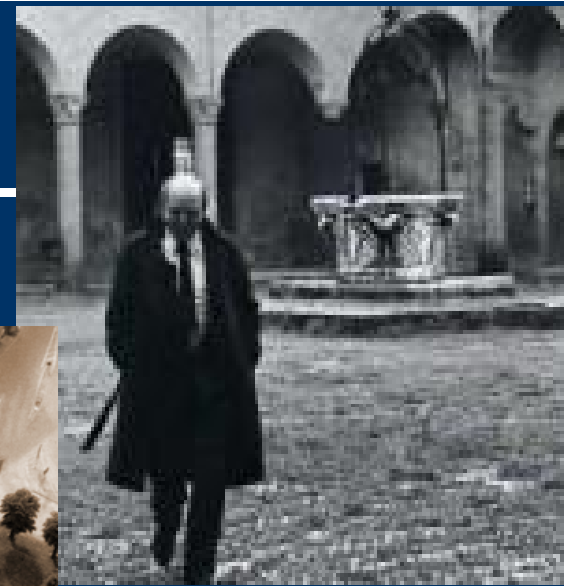
- The **Ramazzini Institute (RI)** is a **non-profit, independent organization** located in Bologna, Italy. It is a cooperative with more than 26,000 active associates.
- Our work principally involves anti-cancer strategies based on cancer prevention.

RAMAZZINI INSTITUTE: THE AIMS

The **aims** of the Ramazzini Institute are:

- **Implementing** schemes of tumor prevention by a strategy based on **promotion of scientific research**
- **Training** specialised staff
- **Circulating information** on environmental and work-related cancer risks and other diseases
- **to set up clinical programmes** of early tumor diagnosis

The CMCRC (1969)



Cesare Maltoni
(1930-2001)



Castle built on 1475
Domus Jucunditatis
of Bentivoglio family



History.....



...and science



h465227 [RM] © www.visualphotos.com



The Glyphosate case

➤ **IARC** (WHO), March 2015

PROBABLE CARCINOGEN (Group 2A)

➤ **EFSA** (EU), October 2015

***UNLIKELY TO POSE A CARCINOGENIC
HAZARD TO HUMANS***

JECH Online First, published on March 3, 2016 as 10.1136/jech-2015-207005

Commentary

Differences in the carcinogenic evaluation of glyphosate between the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA)

Christopher J Portier,¹ Bruce K Armstrong,² Bruce C Baguley,³ Xaver Baur,⁴ Igor Belyaev,⁵ Robert Bellé,⁶ Fiorella Belpoggi,⁷ Annibale Biggeri,⁸ Maarten C Bosland,⁹ Paolo Bruzzi,¹⁰ Lygia Therese Budnik,¹¹ Merete D Bugge,¹² Kathleen Burns,¹³ Gloria M Calaf,¹⁴ David O Carpenter,¹⁵ Hillary M Carpenter,¹⁶ Lizbeth López-Carrillo,¹⁷ Richard Clapp,¹⁸ Pierluigi Cocco,¹⁹ Dario Consonni,²⁰ Pietro Comba,²¹ Elena Craft,²² Mohamed Aqiel Dalvie,²³ Devra Davis,²⁴ Paul A Demers,²⁵

supports that substance's potential to cause or not cause cancer in humans.

For Monograph 112,² 17 expert scientists evaluated the carcinogenic hazard for four insecticides and the herbicide glyphosate.³ The WG concluded that the data for glyphosate meet the criteria for classification as a *probable human carcinogen*.

The European Food Safety Authority (EFSA) is the primary agency of the European Union for risk assessments regarding food safety. In October 2015, EFSA reported⁴ on their evaluation of the Renewal Assessment Report⁵ (RAR) for glyphosate that was prepared by the Rapporteur Member State, the German Federal Institute for Risk Assessment (BfR). EFSA concluded that 'glyphosate is unlikely to pose a carcinogenic hazard to humans and the evidence does not support classification with regard to its carcinogenic potential'. Addendum 1 (the

RAMAZZINI: A NEW STUDY ON GLYPHOSATE

- To resolve the scientific uncertainty over glyphosate, in May the Ramazzini Institute will be starting a pilot experimental study in rats
- On glyphosate alone and one of its most common formulate
- The pilot study is preparatory to a comprehensive long-term (3-year) toxicological study on reproduction, neurotoxicity and carcinogenesis, including low doses, which we are planning to start by mid-2017.

The Glyphosate case

Our experimental project includes the following end-points:

Phase	Arm of the study (*)	End-points/investigations
Preliminary	- Dose-range finding (DRF)	<ul style="list-style-type: none"> • Histopathology • Molecular biology of target tissues • Urine analysis • Biochemical and haematological evaluation
	- Sub-chronic toxicity (Treatment: from GD 6 to PND 90)	
	- Reproductive/Developmental Toxicity	
Main integrated study	- Chronic toxicity/carcinogenicity (Treatment: from GD 6 to 104-130 weeks of age)	<ul style="list-style-type: none"> • Microbiome investigations • Metabolite detection in blood/serum and urine • Breeding, conception and neonatal parameters • Markers of sexual development • Sperm aneuploidy, sperm parameters
	- Mechanistic studies	
	- Reproductive/Developmental Toxicity in specific Windows Of Susceptibility (WOS)	

(*) : GD: gestational day; PND :post natal day

The Glyphosate case

- The **comprehensive and integrated study design** for Glyphosate and its formulate is consistent for detecting all risks related to the exposure of the general population, including embryo and children
- All the ***in vivo phase*** is performed in the same laboratory at the Ramazzini institute in Italy; this avoids bias and gives comparable results for the different end points
- The different end-points are planned to be studied in outstanding facilities in the specific field (metabolomic, molecular biology, hormonal disturbances, etc.)
- An adequate and solid risk assessment will be feasible

The Glyphosate case

- **Scientific uncertainty only generates confusion, waste of energy and money, and no benefit to public health**
- **Whatever the outcome of the Ramazzini Institute study, the regulatory agencies and policy-makers will at last have solid independent results on which to base a proper risk assessment**

Avoid repeating mistakes of the past!

Agent/Compound	CMCRC-RI*	IARC Group/year	Predictivity
Vinyl Chloride	1974	1 /1979	5 years
Formaldehyde	1989	1 /2012	23 years
Trichloroethylene	1986	1 /2014	28 years
Benzene	1979	1 /2012	33 years
MTBE	1995	3 /1999	?
Aspartame	2005	?	?

***first evidence as multipotent carcinogen**

THE "COSTS" OF RESEARCH



"The high costs [human and economic] probably represent the reason why, in the field of experimental and environmental carcinogenesis, words overlap facts, opinions overlap data, and meetings and commission reports submerge good laboratory work."

Cesare Maltoni

A handwritten signature in cursive script, likely belonging to Cesare Maltoni.

From:

Maltoni, C., Lefemine, G., Ciliberti, A.

Carcinogenicity bioassays of vinyl chloride monomer: A model of risk assessment on an experimental basis(1981) Environmental Health Perspectives, Vol. 41, pp. 3-29.