De morbis artificum diatriba, (1700)

Carpi, 1633 – Padua, 1714
De morbis artificum diatriba, (1700)
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.
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 CMCR C (1969)

Castle builted on 1475

Domus Jucunditatis
of Bentivoglio family

Cesare Maltoni
(1930-2001)
History
....and science
The Glyphosate case

IARC (WHO), March 2015
*PROBABLE CARCINOGEN* (Group 2A)

EFSA (EU), October 2015
*UNLIKELY TO POSE A CARCINOGENIC HAZARD TO HUMANS*
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 Belle,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 Del Rosario Dolk,26 Anthony L Dorrington,27 Angela R Draper,28

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
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.
Our experimental project includes the following end-points:

<table>
<thead>
<tr>
<th>Phase</th>
<th>Arm of the study (*)</th>
<th>End-points/investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preliminary</td>
<td>- Dose-range finding (DRF)</td>
<td>• Histopathology</td>
</tr>
<tr>
<td></td>
<td>- Sub-chronic toxicity</td>
<td>• Molecular biology of target tissues</td>
</tr>
<tr>
<td></td>
<td>(Treatment: from GD 6 to PND 90)</td>
<td>• Urine analysis</td>
</tr>
<tr>
<td></td>
<td>- Reproductive/Developmental Toxicity</td>
<td>• Biochemical and haematological evaluation</td>
</tr>
<tr>
<td>Main integrated study</td>
<td>- Chronic toxicity/carcinogenicity</td>
<td>• Microbiome investigations</td>
</tr>
<tr>
<td></td>
<td>(Treatment: from GD 6 to 104-130 weeks of age)</td>
<td>• Metabolite detection in blood/serum and urine</td>
</tr>
<tr>
<td></td>
<td>- Mechanistic studies</td>
<td>• Breeding, conception and neonatal parameters</td>
</tr>
<tr>
<td></td>
<td>- Reproductive/Developmental Toxicity in specific Windows Of Susceptibility (WOS)</td>
<td>• Markers of sexual development</td>
</tr>
</tbody>
</table>

(*) : 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.
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!

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

*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

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