MINISTRY OF INDUSTRY AND TRADE OF RUSSIA

GMP VIII ALL-RUSSIA GMP CONFERENCE

50 years GXP SID& GP

Practical Implications of Introducing Risk Assessment of Elemental Impurities

Regulatory Requirements

Decision of Board of the Eurasian Economic Commission No. 138 dated October 04, 2022 On Approval of the Requirements for Conducting Research (Testing) of Medicinal Products in Terms of Assessing and Monitoring the Content of Impurities

In accordance with Article 6, Paragraph 7 of Article 7 and Article 13 of the Agreement on Common Principles and Rules for the Circulation of Medicines within the Eurasian Economic Union as of December 23, 2014, as well as in order to establish uniform approaches to the assessment of safety and quality of medicinal products and to determine acceptable levels of impurities in medicinal products, the Board of the Eurasian Economic Commission decided:

1. To approve the attached Requirements for conducting research (testing) of medicinal products in terms of assessing and monitoring the content of impurities.

2. This Decision shall come into force 6 months after the date of its official publication.

Chairman of the EEC Board M. Myasnikovich

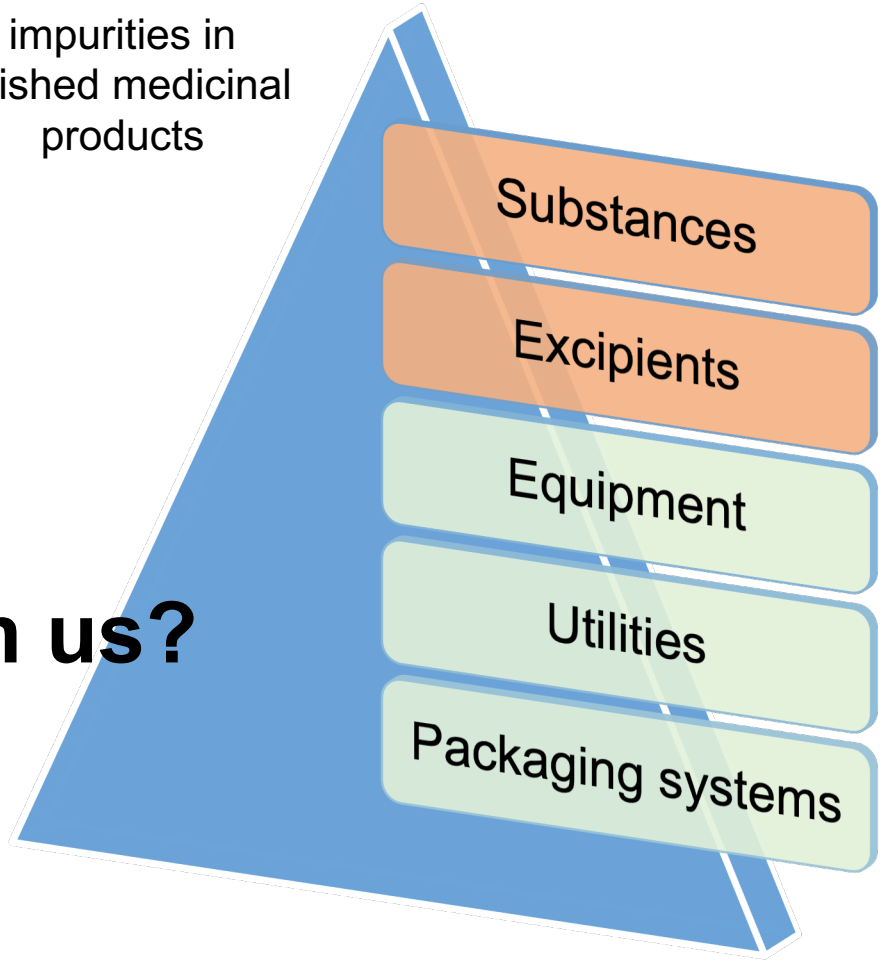
APPROVED by
Decision of Board of the Eurasian Economic Commission
No. 138 dated October 04, 2022

Assessing sources of impurities

Equipment, utilities, packaging systems of a **manufacturer of finished products:**

- Designed to meet GMP requirements;
- Subject to regular monitoring;
- Can be assessed and analyzed by the manufacturer;
- There is no doubt about the identity and composition of impurities.

Elemental impurities in finished medicinal products



What might be hidden from us?

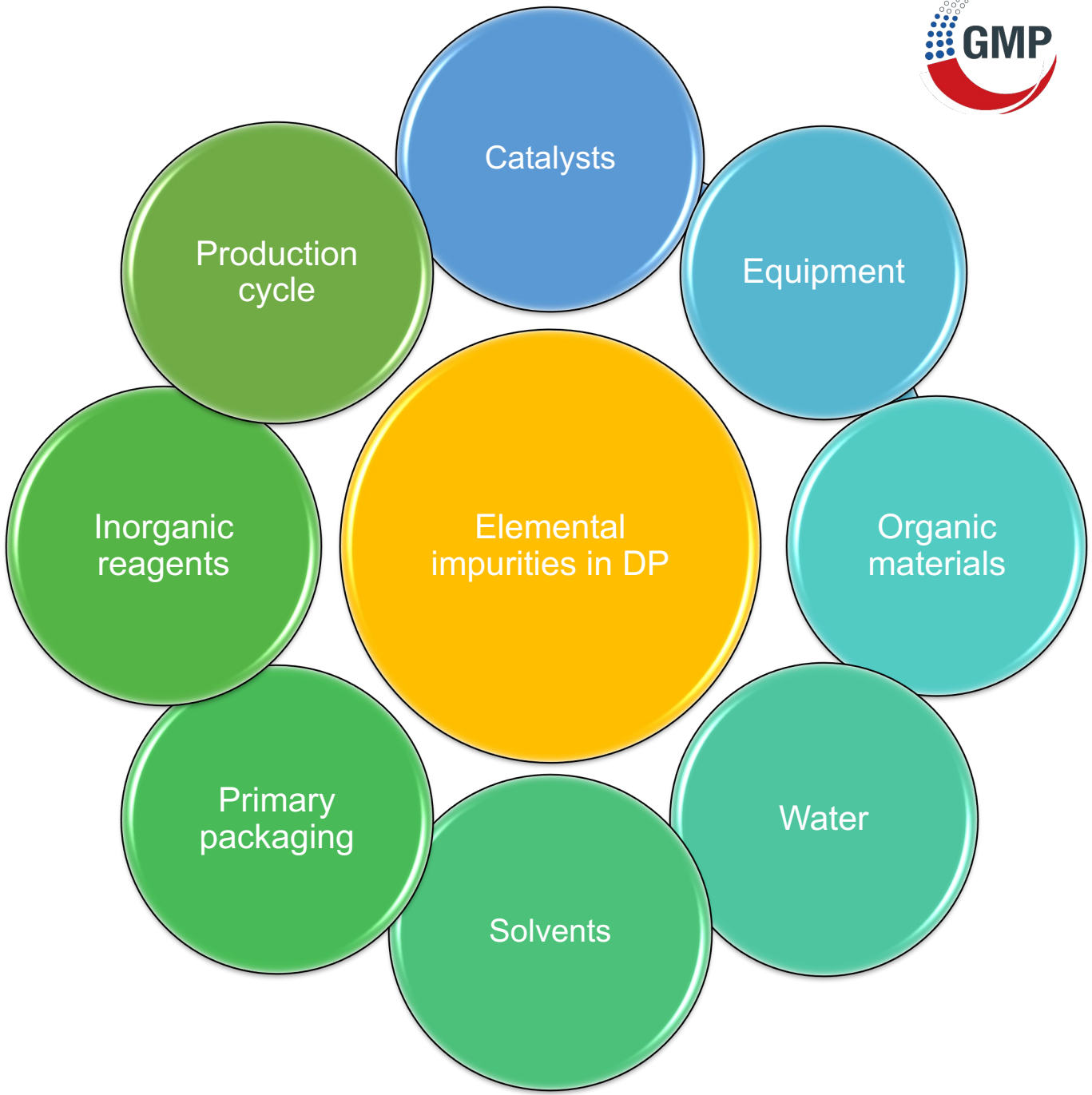
- Excipients
- Active pharmaceutical ingredients

APIs

One of the key components of a medicinal product:

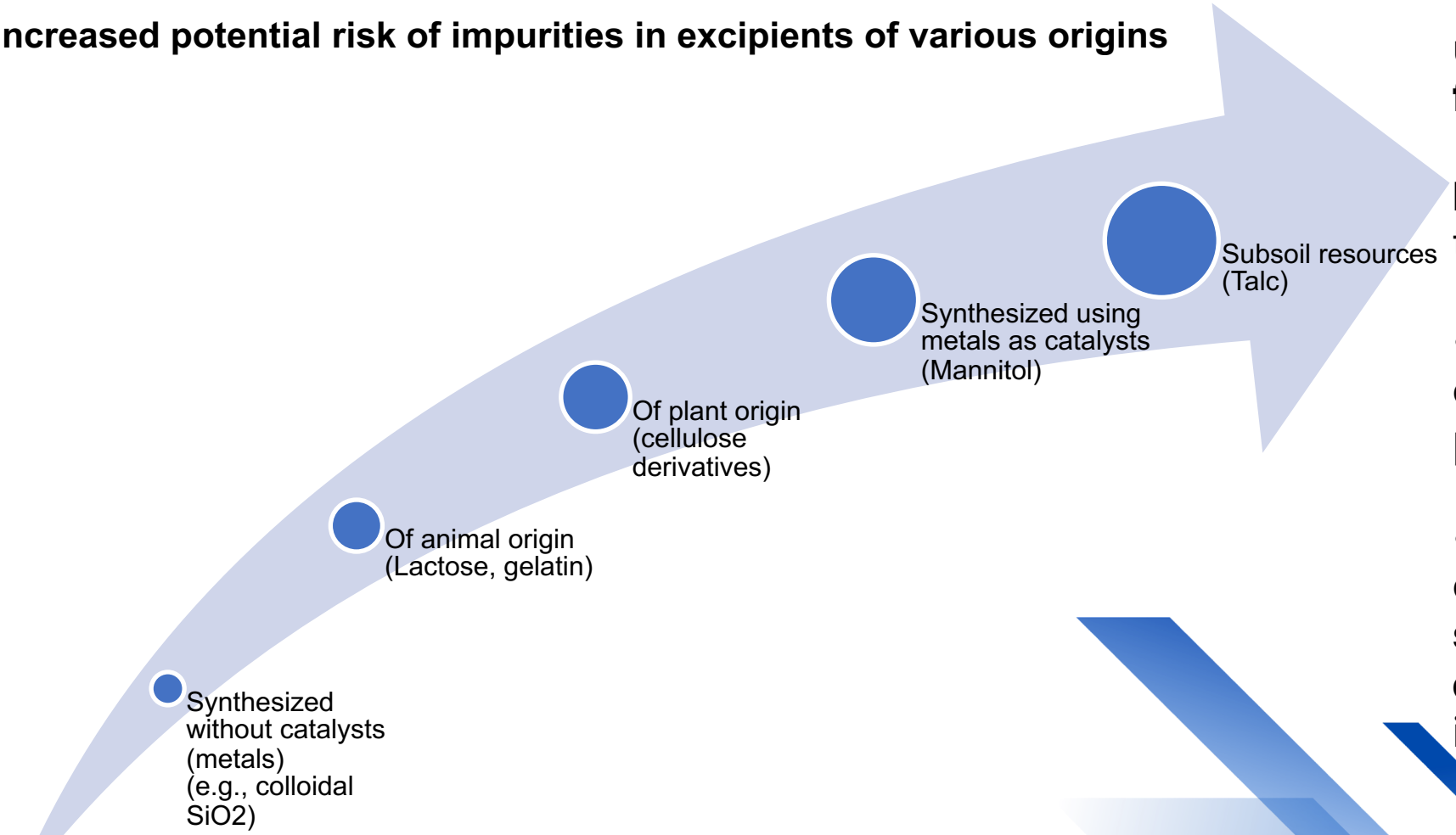
- **The highest risk** comes from intentionally added metals, catalysts for chemical reactions used in the process, especially in the final stages;
- Other sources of contamination make a minor contribution but should be assessed;

- Most of the possible sources of metals are also characteristic of excipients



Excipients

Increased potential risk of impurities in excipients of various origins



The amount of excipient used is an **important factor**.

Elemental impurities that require attention:

- **Class 1 and Class 2a** elements potentially present in trace amounts,
- **Class 3** elements from excipients **intended for a specific route of administration** (e.g., inhalation).

What does this mean for a pharmaceutical manufacturer?

- We are responsible for regulatory compliance;
- The pharmaceutical sector is not the main market for an excipient manufacturer;
- The natural desire to alter the specification for excipients does not always coincide with the excipient manufacturer's capabilities or desire;
- Excipient manufacturers do not test each batch for elemental impurities, moreover, the metal content of many excipients is in the range of 1-10 ppm, and therefore we do not have accurate data;

How can we get the information we need?

- Knowledge of the manufacturing process;
- Publications in literature, scientific journals, articles, etc.;
- Information from material manufacturers and suppliers;
- **Data obtained from testing at incoming control (substances, excipients);**
- Data obtained from testing of finished medicinal products.

Good information is hard to come by.
It's even harder to do anything with it.
Robert Lynn

Conclusion:

- Practical implementation of this guideline needs continuously updated information, which requires interaction of several parties, not only interaction between the **manufacturer** of finished medicinal products and its suppliers;

- It is worth considering the establishment of a knowledge base on this subject, including the information on process aids, manufacturers and test results.

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