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Assessment of Elemental Impurity Exposure and Regulatory Compliance in Benzonatate Capsules

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ABSTRACT: The source of the elemental impurity in drug products might come from API, excipients, manufacturing equipment, water and container closure system. The element impurities in drug products must be controlled, in order to safeguard patient safety and comply with the regulatory guidance. The present report was designed to evaluate the elemental impurity risk assessment of Benzonatate Capsules USP 100 mg in accordance with the guideline Q3D of ICH. The potential sources that contain elemental impurities were evaluated with the application of vendor declarations, certificates of analyses and also supplemented by analytical test data where available. It is determined the contribution from Class 1, Class 2A, and respective Class 2B elements within their corresponding permitted daily exposure (PDE) limits at oral administration. Contribution to elemental impurities from the manufacturing equipment, purified water, processing materials, container closure systems have also been evaluated. In summary, potential contribution to the element impurity has been found not to exceed its permitted safety limit and also below the 30% of PDE control limit, thus additional controls has not been deemed to be needed.

INTRODUCTION

Components of drug products, processing equipment, container/closure systems, residual catalysts included on purpose during synthesis, and other interactions can all result in elemental contaminants being present in medication products. This recommendation consists of three parts: the assessment of the toxicity information for possible elemental contaminants. An application is not required to firmly establish the constraints according to process capacities, as long as the elements does not exceed the PDEs contaminants in pharmaceutical items. Lowering elemental impurity levels may occasionally be justified if they have been demonstrated to affect other drug product quality aspects (such as element-catalyzed drug substance breakdown) at levels below toxicity limits. Furthermore, it is important to check additional criteria (such as ICH Q3A) and take into account other limitations when it comes to pharmaceutical quality for elements with high PDEs. Elements present in the environment or employed or introduced in the production of medicinal compounds or excipients are referred to as elemental impurities for pharmacopeial purposes. Instead of using the vague term "heavy metals," we will use the term "elemental impurities," which includes a variety of transition metals and metalloids. Minerals used in the production of excipients, container-closure systems, and other product contact surfaces are potential sources of elemental contaminants in medicines, in addition to catalysts or reagents typically utilized in chemical synthesis. The elements that realistic manufacturing procedures are unable to entirely eliminate are known as elemental impurities, and they should be assessed in light of safety-based limitations. According to ICH Q9's risk management guidelines, this guideline outlines a procedure for evaluating and managing elemental impurities in

pharmaceutical products. In order to lower the therapeutic product's elemental contaminants, this procedure offers a foundation for creating a risk-based control plan [1][6].

SCOPE

The guideline is applicable to both new drug products that comprise existing drug ingredients and new completed ICH Q6A and Q6B definitions for drug goods were used. Drug items that are utilized in the clinical research phases of their development are exempt from this recommendation. The guidelines' tenets can be helpful in assessing potential elemental contaminants in novel pharmaceutical products when the commercial process is established.

EVALUATION OF POTENTIAL ELEMENTAL IMPURITIES FOR SAFETY

1.The Routes of Administration: Oral, Parenteral, and Inhalation: Overview of Safety Assessment Guidelines for Elemental Impurities

The components of this guideline that were evaluated were examined through a review of data that was made publicly available internationally recognized regulatory standards, government research reports, and scientific journals and guidance that apply to drug products, and research and assessment reports from regulatory authorities. The following ICH Q3C principles are adhered to in this process: Final Solvents.

The following is a summary of the elements that were taken into account during the safety evaluation to determine the PDE, roughly arranged by relevance:

- Human exposure and safety data where available;
- The element's expected oxidation state in the therapeutic product;
- The most important animal research;
- the administration route;
- the appropriate endpoints.

2. Different Administration Methods

Parenteral, inhalation, and oral delivery methods all had PDEs developed. The ideas outlined in this guideline may be utilized to develop PDEs when they are required for alternative routes of administration. An existing PDE may rise or fall as a result of an assessment.

- Determine whether the elemental contamination is anticipated to cause local consequences when supplied using the planned administration route.
- In the event that local anticipated, determine whether an existing PDE has to be modified.
- Take into account the anticipated dosages and exposure levels for these effects in relation to the adverse effect that served as the benchmark for an established PDE.
- No modification to a well-known PDE is required in the event that local effects are not anticipated.

3. Parenteral Products

The maximum daily volume of parenteral medicinal products, up to a maximum of two liters, can be utilized to determine tolerance levels from PDEs.

4.ELEMENT CLASSIFICATION

Considering their potential for toxicity (PDE) and the probability that occurring within the pharmaceutical product, the constituents covered in this guidance have been divided into three types. The probability of the element being used in pharmaceutical processes, the likelihood that it will co-isolate with other elemental contaminants in substances utilized in pharmaceutical manufacturing, its documented natural abundance, and its environmental dispersion are some of the factors that determine its likelihood of occurring.

Class 1: Since Pb, Cd, and Hg are toxicants to humans with little to no use in the synthesis of pharmaceuticals. Usually derived from widely used materials (such as mining excipients), they are found in pharmaceutical goods. These four elements which have unique properties—must be included During the risk assessment procedure, together with all potential sources and routes of administration for elemental impurity.[6]

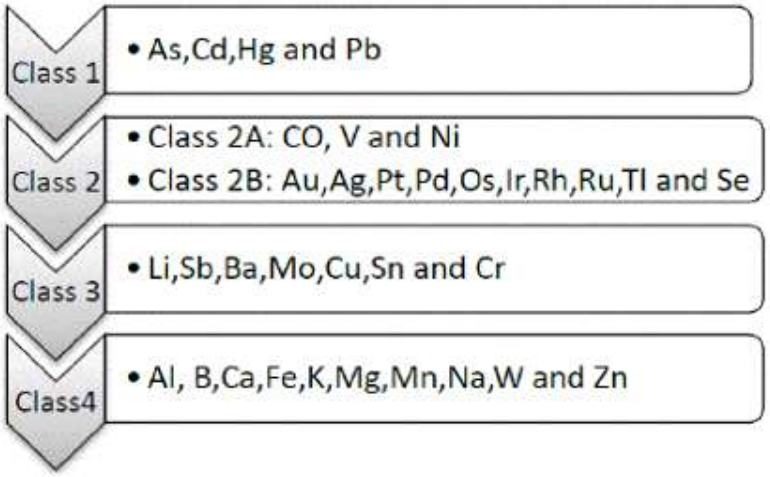
Class 2: Most substances in this class are regarded as poisons to humans that depend on the path. Sub-classes 2A and 2B are created from Class 2 elements according to how likely it is that they will appear into the pharmaceutical substance.

Class 2A: Because of the comparatively high likelihood of elements being in the therapeutic product, risk analysis is required for every possibility sources of elemental contaminants as well as administration methods. Co, Ni, and V are the elements of class 2A.

Class 2B: Because of their low abundance and poor capacity for co-isolation with other materials, elements have a lower Possibility of existing in the pharmaceutical medication. Not unless they are purposefully included When the drug's ingredients, excipients, or other components are being manufactured, they may therefore be left out of the evaluation of risk. Ru, Se, Ti, Ag, Au, Ir, Os, Pd, Pt, Rh, and Ru are among the elemental impurities in class 2B [9].

Class 3: Although components this class have comparatively mild oral poisonous substances and substantial PDEs (typically larger than 500 μg/day), they would still need to be considered when assessing the hazards associated with parenteral and inhalation routes. Unless the PDE specific to the route exceeds 500 μg/day, parenteral and inhalation products should evaluate the risk of having elemental contaminants during the risk evaluation. It is necessary to conduct this assessment for oral delivery methods. The following components are part of this class: Mo, Sb, Sn, Li, Ba, Cr, Cu, and Li.

ELEMENT CLASSIFICATION



A. General Principles

• Determine the known and potential sources of any elemental contaminants that might infiltrate the medicinal product.

• Assess whether a certain elemental impurity is present in the pharmaceutical product by contrasting the PDE with the observed or predicted amount of the contaminant.

• Summarize and write the risk assessment.

• Determine whether the process's built-in controls are adequate or what additional controls should be taken into account to reduce elemental contaminants in the medicinal product.

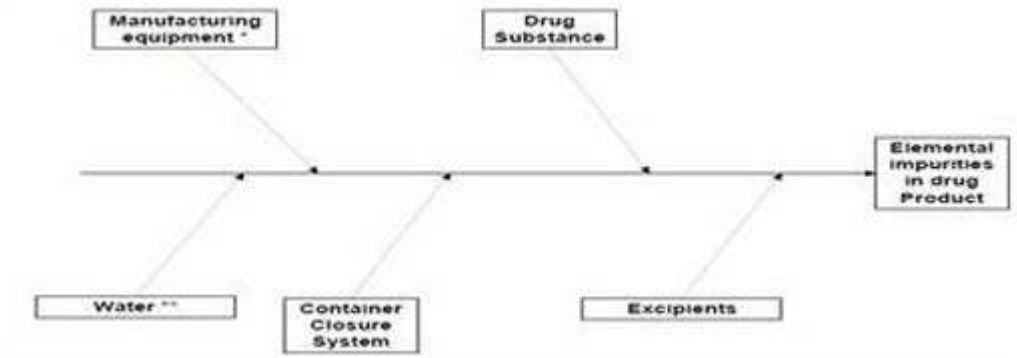
B. Various Sources of Impurities in Elements

• Any residual contaminants left over after components (such catalysts) were purposefully Excipients, or additional pharmaceutical product ingredients, were manufactured and added to the drug substance.

• Unintentionally added elemental impurities that may be detected and taken into consideration if they are found in the drug material, water, or excipients utilized to prepare the drug product in the drug substance's risk evaluation.

• Potentially included elements from manufacturing equipment that could find their way into the drug substance or drug product.

• Component contaminants that could leak from container sealing systems into the drug material and 301 drug products [1].



C. Determining Possible Elemental Impurities

Possible elemental contaminants resulting from catalysts and inorganic chemicals that have been purposefully added:

Any purposeful addition of an element should be taken into account in the risk assessment. In this category, it is easy to characterize and establish methods for regulating the elemental impurities and to identify the probable impurities.

Possible elemental contaminants found in medication ingredients and/or excipients include:

Certain pharmacological compounds and/or excipients may include some elemental impurities, even if they are not purposefully added. The risk evaluation should take these factors' potential inclusion in the drug product into account.

Possible constituent contaminants originating from manufacturing machinery: The percentage elemental contaminants from this source could be small, and the specific manufacturing equipment used to produce the drug product will determine the risk evaluation, a subset of elemental impurities should be included.

Leaching elements from container closing systems: Founded on a knowledge of science concerning the probable exchanges between a specific medication product type and its container, elemental contaminants It is important to identify any that container closure systems might introduce. There is no need to conduct an additional risk assessment when an examination of the building materials shows that the container closing system is free of elemental impurities. Usually, when the medication product's Closing system for containers is being evaluated, this source of elemental contaminants will be addressed.

Important to take into account the following factors (for dosage forms that are liquid or semi-solid):

• 365 ionic content and hydrophilicity/hydrophobicity

• Temperature (cold chain in relation to processing conditions and ambient temperature)

• pH

• Composition of the component or container; terminal sterilization; and packaging technique.

METHODOLOGY

There are two ways to calculate each elemental impurity's (EI) maximum daily exposure.

(i)According to vendor and supplier assertions;

(ii)Result of each component EI screening.

The computed mean difference of every each person's EI is contrasted with the EI's PDE restrictions as specified in ICH Q3D in order to confirm conformity with the specific administrative route. The actions are frequently taken into consideration at the

same time. Taking into account the findings of the risk assessment, the ultimate strategy should be designed to guarantee that the EIs do not beyond the PDE.

Method I

Using the vendor/supplier statements that are available, In a formulation, the MDE for every EI is determined in this way:

1. Utilizing the maximum daily dosage (MDD) of the medication product, compute each constituent's amount (per dosage unit) to determine the total daily intake (TDI) in grams (g).

2. Multiply the weight (in ounces) of every one TDI element from the vendor's certificate of analysis/statement by the specified value of EI (µg/g) is the highest value allowed. is utilized for computation). This gives the daily µg of the ingredient's EI.

3. To obtain the Total µg of each EI per day is the MDI, add up the person amounts (the µg/day) acquired for each medicinal product element in step 2.

4.Carry out the previously described MDI computation for each questionable EI, and a comparison the findings with the daily exposure to EI allowed by ICH Q3D.

Method II

The following formula is used to ascertain the MDI for every EI in a formula. using the generated analytical data:

1. Convert the EI level of each product in µg/g to µg for the entire daily consumption (MDI). Increase by the product's weight (in grams per day) by the EI (µg/g) value to determine the maximum amount of EI that can be consumed each (µg).

2. Carry out the forementioned MDI computation for every EI that is of worry, and contrast the results with the ICH Q3D-listed EI PDE.

3. Whether these elements are intentionally added as a catalyst or inorganic reagent, whether they could be found in pharmaceutical ingredients and/or excipients, or whether they could be derived These components must to be taken into account in the risk assessment, whether they came from manufacturing processes and equipment or leached from container closing mechanisms [1].

4.USP general chapter does not take into account the elements Cobalt (Co), Thallium (Tl), Gold (Au), Selenium (Se), Silver (Ag), Lithium (Li), Antimony (Sb), Barium (Ba), and Tin (Sn).

5. Should the risk analysis approach reveals no possible EI, then the evaluation of potential EI is considered completed.

6. Documentation of the risk assessment's findings and any supporting data and information is required. Any EI found during the process should have its sources taken into account in the risk assessment, along with any impurities. The evaluation's findings should be documented together with pertinent data.

7. The summary of risk evaluation is produced by analyzing medication product information together with data and expertise to ascertain the important potential EI that may be seen in the medicinal goods.

8. The synopsis need to take into consideration the importance of what is seen or anticipated EI level in connection to the EI PDE.

9. A control threshold of thirty percent of the drug product's established PDE should be established for the detected significant EI level [3].

10. Additional controls may not be necessary if the total EI level of the medicinal product across all sources is predicted to be consistently less than 30% of the PDE, given that the data is properly evaluated and show sufficient controls on EI.

11.Controls to guarantee the evaluation of risks. If it is not possible to show that an EI level is continuously below the control threshold, then measures should be taken to ensure that the EI level in the drug product does not surpass the PDE.

12.Micrograms per day (µg/day) are used to report the PDE of each EI that may be present in a product's maximum daily consumption [3][1].

13.The PDE can be converted into concentrations, which only capture An essential technique for evaluating EI in medicines or the components that make them is to look at the overall exposure from the drug product.

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14. The following alternatives outline A few reasonable methods for determining EI concentrations in pharmaceutical items or their constituent parts that guarantee the drug product doesn't surpass the PDEs.

Option 1: When a maximum of 10 grams of the medication product are consumed each day. **Option 2A:** For a drug product with a set daily intake, common allowed concentration limits across drug product components.

Option-2B: Allowed concentration limits of constituents in distinct product components with a designated daily consumption [4].

Option-3: Finished product analysis.

Table1: Quantitative composition for Benzonatate Capsules, USP 100mg

Name of the components	References	Function	mg/capsule	% of the final Capsule weight	Maximum daily intake
Capsule fill:					
Benzonatate	**USP**	Cough suppressant	100.000	53.420	0.6
Fill Weight:			**100.000**	**53.420**	**0.6**
Capsule Shell:					
Gelatin	**NF**	Stabilizer,thickener	53.605	28.635	0.321
Glycerin	**USP**	Humectant	23.746	12.685	0.142
Methyl Paraben	**NF**	Preservative	0.139	0.0742	0.0008
Propyl paraben	**NF**	Preservative	0.0346	0.0184	0.0002
Name of the components	**References**	**Function**	**mg/capsule**	**% of the final Capsule weight**	**Maximum daily intake**
D&C Yellow No10	**IH**	Colorant	0.0785	0.0419	0.0004
Purified water	**USP**	Solvent	9.592	5.124	0.0575
Total capsule Shell Weight:			**87.195**	**46.579**	**0.5229**
Total Weight of the capsule:			**187.195**	**99.999**	**1.1229**

Miscellaneous

S.No	Materials	Reference	Vendor	Function	Quantity/Capsule

1.	Medium Chain Triglycerides	NF	**AAK India Pvt Ltd**	Capsule shell Ribbon Lubricant	Traces
2.	Isopropyl Alcohol	USP	**Avantor Performance Material Ltd**	Cleaning the capsules and wiping of dried capsules	NA
3.	Nitrogen	NF	**Arumugamvelu Air Products**	Purging &Blanketing	Traces
4.	Wiping Cloth	IH	**SV Enterprises**	Cleaning the capsules and wiping of dried capsules	Wiping

Table 2: Container Closure Systems

S.No	Pack size	Vendor Name	Packaging Material
1.	100's	**Shriji Polymers India Pvt Ltd**	**Container-**60CC HDPE Bottle with 33MM Neck
			Cap-CR Closure 33with liner-Alkem
2.	500's		**Container-**200CC HDPE Bottle with 38MM Neck
			Cap-38MM PP CR Closure -Alkem

Table3: Identification of potential elemental impurities from the potential sources

Potential source of elemental impurities	Information evaluated	Further consideration in the risk Assessment
Drug Substance Benzonatate	Vendor declaration on elemental impurities	API vendor has conducted elemental testing. Same data is used for risk evaluation
Excipients	Vendor certificate of analysis specification and declaration	Each excipient was considered a component in calculation of elemental impurities
Purified Water	The purified water is used during manufacturing &cleaning process and quality control department ensures conformance with USP/IP/BP/Ph.Eur.Hence,it doesn't possess any risk.	No further consideration in the risk assessment.

Potential source of elemental impurities	Information evaluated	Further consideration in the risk Assessment
Container closure system	According to the vendor's statement, no components were purposefully introduced during the production of HDPE containers and closures. As a result, elemental contaminants from container closure have very little effect on the medication product.	No further consideration in the risk assessment
Manufacturing equipment (drug product equipment)	Mainly two types of stainless steel were used in production equipment manufacturing SS316 used to construct the equipment components those get in direct product contact and SS304 is used for the non contact parts. As a part of qualification of equipment	No further consideration in the risk assessment
Manufacturing equipment (drug product equipment)	MOC verification was done. The manufacturing equipments were subjected to routine preventive maintenance and calibration program. SS316 does not react with the product ingredient. Hence the manufacturing process of benzonatate capsules 100mg is less likely to degrade the equipmnent contact surface area ensuring neligible contribution from drug processing equipment detailed information about manufacturing equipment for consideration during the risk assessment is provided in table4.	No further consideration in the risk assessment
Medium chain triglycerides	From the declaration of elemental impurities states that there are no metal catalysts &no more metal impurities likely to arise from other sources like raw materials and equipments.so it poses no risk on the finished product.	No further consideration in the risk assessment
Isopropyl alcohol	Isopropyl alcohol is used in the wiping stage of capsule and it is controlled with a specification of not more than 1000 ppt by a validated analytical method.	No further consideration in the risk assessment
Wiping cloth	Lint free wipes is generally used for wiping hence it doesn't possess any	No further consideration in the risk

	risk.	assessment
Nitrogen	Nitrogen is used for purging during manufacturing process hence it doesn't possess any risk.	No further consideration in the risk assessment

Table4: Risk Assessment for equipments

Equipment	Process	Material	GMP controls	Final risk assessment
Weighing balance	Verification of raw materials	SS316	Covered by routine Good Manufacturing Practice (Maintenance ,Cleaning ,etc)	No risk
Gelatin melting tank	Melting of gelatin and mixing of shell materials	SS316	Covered by routine Good Manufacturing Practice (Maintenance ,Cleaning ,etc)	No risk
Encapsulation machine	Encapsulation	SS316	Covered by routine Good Manufacturing Practice (Maintenance ,Cleaning ,etc)	No risk
Tumble drier	To dry the capsule	SS316	Covered by routine Good Manufacturing Practice (Maintenance ,Cleaning ,etc)	No risk
Wiping pan	To wipe the capsule	SS316	Covered by routine Good Manufacturing Practice (Maintenance ,Cleaning ,etc)	No risk
Metal detector	To detect the presence of any metals	SS316	Covered by routine Good Manufacturing Practice (Maintenance ,Cleaning ,etc)	No risk
Sorting machine	Sorting of capsules	SS316	Covered by routine	No risk

			Good Manufacturing Practice (Maintenance ,Cleaning ,etc)	

Equipment	Process	Material	GMP controls	Final risk assessment
Inspection table	To visually inspect the capsules	SS316	Covered by routine Good Manufacturing Practice (Maintenance ,Cleaning ,etc)	No risk
Dedicated hose	To carry fluids	SS316	Covered by routine Good Manufacturing Practice (Maintenance ,Cleaning ,etc)	No risk
Laser printing machine	Printing	SS316	Covered by routine Good Manufacturing Practice (Maintenance ,Cleaning ,etc)	No risk

RESULTS

Permitted daily exposure for oral administration as per ICH Q3D Drug substance

- Benzonatate by Siegfried Evalonnaz SA is used as Active Pharmaceutical Ingredient in the formulation of the drug product.
- As per vendor declaration analytical testing was performed by validated ICP-MS method and palladium was intentionally added. Element
- The contribution of an elements into drug product is assessed and depicted in the below table

1.Elemental impurities -expected contribution from Benzonatate

Element	Class	PDE	Element concentration in drug substance in microgram/g
Cd	1	5	0.15
Pb		5	0.15
As		15	0.45
Hg		30	0.9

Co	2A	50	1.5
V		100	3
Ni		200	6
Pd	2B	100	3

Excipients (Gelatin NF)

- Gelatin NF (Gelita 160 Bloom Bovine Bone Gelatin Type B)
- Gelatin provided by Gelita used as an excipient in the medication product's composition.
- As per vendor declaration the contribution of an element from gelatin into the drug product is assessed and depicted in the table 2.

2.Elemental impurities -expected contribution from Gelatin

Element	Class	PDE	Element concentration in Gelatin microgram/g
Cd	1	5	0.01
Pb		5	0.05
As		15	0.1
Hg		30	0.005
Co	2A	50	0.1
V		100	0.2
Ni		200	0.1

Glycerin

- Glycerin provided by Godrej industries is used an excipient in the medication product's composition.
- As per vendor declaration Class 1 and Class 2 elements as included in ICH Q3D do not have likely to be present.
- The contribution of an element from glycerin into the drug product is assessed and depicted in the table 3.

3.Elemental impurities -expected contribution from Glycerin

Element	Class	PDE	Element concentration in Glycerin microgram/g
Cd	1	5	0.00
Pb		5	0.00
As		15	0.00
Hg		30	0.00
Co	2A	50	0.00
V		100	0.00
Ni		200	0.00

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Element	Class	PDE	Element concentration in Propyl Paraben microgram/g
Cd	1	5	0.00
Pb		5	0.00
As		15	0.00
Hg		30	0.00
Co	2A	50	0.00
V		100	0.00
Ni		200	0.00

Methyl Paraben

• Methyl paraben provided by Gujarat organics is used an excipient in the medication product's composition.

• As per vendor declaration analytical testing was performed by ICP method .Class 1 and Class 2 elements as listed in ICH Q3D A are not likely to be present.

• The contribution of an element from glycerin into the drug product is assessed and depicted in the table 4.

4.Elemental impurities -expected contribution from Methyl Paraben

Element	Class	PDE	Element concentration in Methyl Paraben microgram/g
Cd	1	5	0.00
Pb		5	0.00
As		15	0.00
Hg		30	0.00
Co	2A	50	0.00
V		100	0.00
Ni		200	0.00

Propyl Paraben

• Propyl Paraben provided by Gujarat Organics is used an excipient in the medication product's composition.

• As per vendor declaration Class 1 and Class 2 elements as included in ICH Q3D do not likely to be present.

• The contribution of an element from glycerin into the drug product is assessed and depicted in the table 5.

5.Elemental impurities -expected contribution from Propyl Paraben

D&C Yellow No.10

• D&C Yellow No.10 provided by Gujarat Organics is used an excipient used in the medication's composition.

• The contribution of an element from glycerin into the drug product is assessed and depicted in the table 6.[7]

6.Elemental impurities -expected contribution from D&C Yellow No.10

Element	Class	PDE	Element concentration in D&C yellow No. 10microgram/g
Cd	1	5	1
Pb		5	10
As		15	2
Hg		30	1
Co	2A	50	5
V		100	0.00
Ni		200	50

- The risk of elements evaluated risk assessment in pharmaceutical products has taken into account Classes 1 through 2A and 2B components according to their toxicity and probability of happening in the therapeutic goods.
- As a result, additional assessment of the equipment used in the production of medicinal products for the Elements Li, Sb, Ba, Mo, Cu, Sn, and Cr in class three is not necessary.
- Since they are not intentionally added. As stated in the ICH Q3D guideline [10].
- The classification's objective scheme is to focus the risk assessment on the components that pose the greatest risk. that also have a decent likelihood of being included in the oral medicinal product [5].

DISCUSSION & SUMMARY

- Permitted Daily Exposure (PDE) derived under ICH Q3D guidelines has been established to guarantee that, based on daily exposure, the exposure to an element present as an impurity in a therapeutic product is safe.
- Elements of Class 1 and Class 2A impurities have been considered in the risk assessment.
- When the EI level above the predetermined PDEs (control threshold), more steps must be made to guarantee that the level stays below the PDE. The EI level can be managed using the following strategies.
- The process of choosing suppliers of pharmacological substances and excipients involves keeping an eye on the amounts of ethyleneimine (EI) and establishing specifications for these ingredients.
- The choice of production machinery, container closure mechanisms, and water sources that adhere to Good Manufacturing Practice (GMP) and meet compendia standards.
- Adjusting the manufacturing process's phases and putting in place in-process controls so that the drug product's EI falls below the control level.
- Key steps include identifying potential sources of contamination (e.g., raw materials, manufacturing processes), setting permissible limits based on safety guidelines (e.g., ICH Q3D), and conducting analytical testing to verify levels.
- Manufacturers must implement controls to minimize impurities and ensure product safety throughout the lifecycle.
- This assessment ensures that levels of these impurities are within safe limits to avoid health risks to patients.

CONCLUSION

Risk evaluation of elemental impurities in drug products is essential because it provides the information needed to determine each element's existence. This information aids while choosing which production processes, apparatus, closure and container systems,

and excipient types and grades. In order to maintain the appropriate controls through screening, which is a requirement of the law and a step in the filling of pharmaceutical items, the information about elemental impurities is also required. Based on ICH Q3D guideline, FDA guidance -elemental impurity impurities and USP a risk assessment was performed. Since the drug products' total elemental impurities from all of its constituent parts are less than the 30% PDE limit of the elements, no further controls are needed. Additionally, no extra elemental contaminants were added throughout the medication product's production process. To ascertain the likelihood that elemental impurities will be present in Benzonatate 100mg for class 1 and class2A elements in the BENZONATATE CAPSULES USP 100 mg to set up the necessary safeguards to guarantee the pharmaceutical product's quality. This risk assessment will be updated as needed if the procedure is altered or the suppliers of the drug product components are replaced. The effects of the modifications will be assessed. This assessment ensures that the capsules pose minimal risk to patient safety due to elemental impurities. It underscores the importance of rigorous quality control measures during manufacturing to prevent contamination and maintain product quality throughout its shelf life. Regular monitoring and adherence to established safety standards are crucial to ensuring continued compliance and patient well-being.

REFERENCES

[1] Kushwaha, P. (2020). Metallic Impurities in Pharmaceuticals: An Overview. Current Pharmaceutical Analysis, 17(8), 960–968. https://doi.org/10.2174/1573412916999200711151147

[2] Srinivasan, C., Ma, Y., Liu, Y., Wang, Y., Hengst, L., Liu, X., Toth, R., Rodriguez, J., Mohammad, A., Bandaranayake, B. M., Simon, D., Beekman, C., Korang-Yeboah, M., Sivan, S., Lee, S., & Cruz, C. N. (2019). Quality attributes and evaluation of pharmaceutical glass containers for parenterals. International Journal of Pharmaceutics, 568, 118510. https://doi.org/10.1016/j.ijpharm.2019.118510

[3] Chawla, R. K., Panda, S., Umasankar, K., Panda, S. P., & Damayanthi, D. (2019). Risk assessment, screening and control of elemental impurities in pharmaceutical drug products: a review. Current Pharmaceutical Analysis, 16(7), 801–805. https://doi.org/10.2174/1573412915666190314144134

[4] Chawla, R. K., Panda, S., Umasankar, K., Panda, S. P., & Damayanthi, D. (2020c). RISK ASSESSMENT, SCREENING AND CONTROLS OF ELEMENTAL IMPURITIES IN PHARMACEUTICAL DRUG PRODUCTS: a REVIEW. RASAYAN Journal of Chemistry, 13(02), 1187–1192. https://doi.org/10.31788/rjc.2020.1325079

[5] Das, P., Kumar, S. V. R., Maity, A., & Oman Pharmaceutical Products Co.LLC. (2018). The recent challenge for the pharmaceutical industries – ICH Q3D Elemental Impurities. In INTERNATIONAL JOURNAL OF PHARMACEUTICS & DRUG ANALYSIS (Vol. 6, Issue 3, pp. 406–418) [Journal-article]. http://ijpda.com

[6] Maithani, M., Raturi, R., Sharma, P., Gupta, V., & Bansal, P. (2019). Elemental impurities in pharmaceutical products adding fuel to the fire. Regulatory Toxicology and Pharmacology, 108, 104435. https://doi.org/10.1016/j.yrtph.2019.104435

[7] Sato, Y., Kutsuna, H., Kobayashi, T., & Mitsui, T. (1984). D&C nos. 10 and 11: chemical composition analysis and delayed contact hypersensitivity testing in the guinea pig. Contact Dermatitis, 10(1), 30–38. https://doi.org/10.1111/j.1600-0536.1984.tb00058.x

[8] Levine, K. E., Ross, G. T., Fernando, R. A., Blake, J. C., Sparacino, C. M., & Pellizzari, E. D. (2004). Trace element content of Senna study material and selected Senna-Based dietary supplements as determined by inductively coupled Plasma-Optical Emission spectrometry and inductively coupled Plasma-Mass spectrometry. Communications in Soil Science and Plant Analysis, 35(5–6), 835–851. https://doi.org/10.1081/css-120030361

[9] Mm, R., Kh, R., & Mu, R. (2016). Harmonized Guideline on Limit and Testing of Elemental Impurities in Pharmaceutical Substances: a review. Pharmaceutical Regulatory Affairs Open Access, 05(02). https://doi.org/10.4172/2167-7689.1000168

[10] Elemental impurities in pharmaceutical excipients. (2015). In Journal of Pharmaceutical Sciences (Vols. 104–104, pp. 4197–4206) [Research article]. Wiley Periodicals, Inc. and the American Pharmacists Association. https://doi.org/10.1002/jps.24650

[11] Elemental impurities in pharmaceutical excipients. (2015). In Journal of Pharmaceutical Sciences (Vols. 104–104, pp. 4197–4206) [Research article]. Wiley Periodicals, Inc. and the American Pharmacists Association. https://doi.org/10.1002/jps.24650

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