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Medicines

REGULATORY NEWS

CMDh highlights

CMDh meeting with Interested Parties - 31 May 2023 – Minutes

The **CMDh published the minutes of the meeting with Interested Parties** that took place on 31 May 2023. The minutes can be accessed here.

The CMDh also published the **minutes of the dedicated CMDh-IP meeting on variations** which are available here.

CMDh minutes - June 2023

The **CMDh published the minutes of the CMDh meeting held on 20-21 June 2023**.

USER TESTING OF THE PACKAGE LEAFLET

The EMA informed the CMDh about the outcome of the QRD discussions on the possibility of virtual/remote user testing of the package leaflet.

QRD agreed that in-person user testing remains the preferred option. However, also virtual/remote user testing can still be allowed. Due to the current legal framework, it was however stressed that a printed version of the package leaflet has to be used during the interview namely to address aspects as the design, layout, quality of paper etc.

PROPOSAL FOR INCLUSION OF INFORMATION ON DISPOSAL IN THE PI FOR TOPICAL MEDICINAL PRODUCTS CONTAINING DICLOFENAC

The CMDh was informed of the NcWP response to the CMDh question on the need to include information on the disposal in the PI for topical medicinal products containing diclofenac.

Following consultation with the SmPC advisory group, the NcWP provided a proposal for a wording to be included in the PI of concerned products. Some concerns on the proposal were raised by some MSs. It was agreed that the CMDh concerns will be summarised for further discussion in July (Action: DE, DK, NO) and will then be sent back to NcWP for further consideration.

CMDh minutes – July 2023

The CMDh published the minutes of its meeting held on 18-20 July 2023. As a complement to what was highlighted the CMDh July meeting report, the following may be noted:

MULTILINGUAL PACKAGING WORKING GROUP

The WG Chair reported from the June 2023 WG meeting. The WG discussed the ongoing pilot on preparation of EU reduced harmonised text, the results of the survey to IPs, plans to update the BPG on MLP and the legislative proposal for the update of pharmaceutical legislation.

LU presented to the WG their experience of moving to joint packs with BE, DE, FR and AT. Some MSs raised concerns to have the LU MA number reflected in their national PI in case of joint packs. LU will provide a list of concerned products and discuss the approach bilaterally with the concerned MSs.

HMA MAWP

The CMDh discussed an action included in the HMA MAWP assigned to CMDh to "conduct and implement "lessons learned evaluation", specifically in MRP/DCP and clinical trials, to promote scientifically supported positions and encourage an attitude of "need to know" rather than "nice to know"."

The CMDh stressed that many actions have already been implemented in the past, e.g. to fully rely on the RMS assessment and to avoid parallel assessments as CMS. Also several templates have already been updated to further facilitate the assessment work. The CMDh agreed to prepare a survey to MSs to enquire e.g. which quality assurance systems are in place at national level. SE will prepare a first draft survey for further discussion in September.

BLISTER PACKS WITH EMPTY CAVITIES – RISK FOR POTENTIAL MEDICATION ERRORS / PATIENT NON-COMPLIANCE

The CMDh agreed by majority with the wording proposed to be included in the QRD stylistic matters guide to address the issue of empty cavities in blister packs. However, the CMDh requested QRD to strengthen the wording that the foil of the blister should indicate which pockets are empty. This was not considered to be an issue with multi-lingual packs as a simple symbol could be used. The CMDh request will be further discussed by QRD.

PROPOSAL FOR INCLUSION OF INFORMATION ON DISPOSAL IN THE PI FOR TOPICAL MEDICINAL PRODUCTS CONTAINING DICLOFENAC

The CMDh agreed comments to be sent back to NcWP on their feedback provided to the CMDh question on inclusion of information on disposal in the PI for topical medicinal products containing diclofenac. The CMDh comments will be sent to NcWP.

BRIDGING REQUIREMENTS FOR WELL-ESTABLISHED USE APPLICATIONS

NL presented the outcome of a questionnaire to Member States on data requirements for well-established use applications, in particular, which bridging studies are needed.

Survey responses showed a different interpretation / implementation of the requirements mentioned in Annex I Part II of Directive 2001/83/EC *("The non-clinical and/or clinical overviews must explain the relevance of any data submitted which concern a product different from the product intended for marketing. A judgement must be made whether the product studied can be considered as similar to the product, for which application for a marketing authorisation has been made in spite of the existing differences*") by MSs.

The CMDh agreed to consult MWP in order to establish a consistent approach among Member States, preferably via guidance. Questions to MWP will be prepared for further discussion in September. The CMDh also stresses to applicants that well-established use applications are strongly discouraged in case a RefMP is available on the market. In such cases, generic applications should be submitted.

CMDh report - July 2023

The CMDh has published the **report from the CMDh meeting held on 18-20 July 2023**. Among the items reported, the following may be noted:

CALL FOR REVIEW FOR CHEMICALLY SYNTHESISED AND BIOLOGICAL MEDICINAL PRODUCTS REGARDING NITROSAMINE IMPURITIES

The CMDh in liaison with EMA and CHMP has agreed an update of the Questions and Answers for MAHs/applicants on the CHMP Opinion for the Article 5(3) of Regulation (EC) No 726/2004 referral on nitrosamine impurities in human medicinal products.

Q&A 10 has been amended to include the Carcinogenic Potency Categorisation Approach (CPCA) and the enhanced Ames test (EAT) for establishing Acceptable Intakes (AIs) for N-nitrosamines. The list of nitrosamines for which AIs have been established by the Non-clinical Working Party (NcWP) has been moved to a new Appendix 1, which includes new AIs for N-nitrosamines determined using the CPCA. Annex 2 and 3 have been added to further describe the CPCA and the EAT conditions.

A further update of Q&A 20 and 21 has been included to remove the universal temporary AI (t-AI), while a formal AI is established, as it is no longer considered necessary. Q&A 22 on the approach to control presence of N-nitrosamine exceeding the AI, while CAPAs are being implemented, has been amended to extend the scope to authorised products for chronic use and clarify the applicable limits and exemptions.

The CMDh and EMA have further updated the template for the notification of step 2 confirmatory testing outcome: confirmation of nitrosamine detected, to reflect the new approaches. *Please see the dedicated website*.

As during the above-mentioned updates new and revised AIs have been published for some nitrosamines, MAHs of products concerned by those nitrosamines are requested to resubmit their step 2 response in the updated template to (re-) confirm under which scenario their products should be classified under the newly published AIs. This is particularly important in case a step 2 scenario A or D response was submitted.

Finally, the CMDh agreed an update of its Practical Guidance for MAHs of nationally authorised products (incl. MRP/DCP) in relation to the Art. 5(3) Referral on Nitrosamines (tracked). As the process for handling nitrosamines is now well-established and AIs can be determined in a timely manner with the CPCA, the CMDh does not consider it necessary anymore to keep procedures in clock-stop due to missing data on nitrosamines. Any outstanding issues related to nitrosamines would have to be addressed before Day 210 of the DCP without the possibility for post-approval commitments.

PHASING OUT OF EXTRAORDINARY COVID-19 REGULATORY FLEXIBILITIES

The CMDh, in line with EMA, the European Commission (EC) and the Heads of Medicines Agencies (HMA), is phasing out the extraordinary regulatory flexibilities for medicines put in place during the COVID-19 pandemic to help address regulatory and supply challenges arising from the pandemic (see also EMA/EC/HMA announcement). This follows the end of the COVID-19 public health emergency declared by WHO in May 2023.
The extraordinary regulatory flexibilities covered different areas, including marketing authorisation and related regulatory procedures, manufacturing and importation of active pharmaceutical ingredients and finished products, quality variations, labelling and packaging requirements and compliance. Also, a series of measures to mitigate the impact of disruptions caused by the public health emergency on inspections of manufacturing facilities or other sites relevant for medicinal products in the EU was agreed during the pandemic. The extraordinary flexibilities ensured the continued availability of medicines while making sure that good manufacturing (GMP) and distribution practice (GDP) standards were being adhered to.

From now on, the regulatory flexibilities that were introduced specifically during the COVID-19 pandemic should no longer be granted. For already approved labelling flexibilities, e.g. the English-only labelling for COVID-19 vaccines, their application will be extended until the end of 2023, in order to ensure a smooth phase-out and avoid any supply difficulties or other disruptions due to a sudden change in applicable requirements. After 2023, the regular mechanisms foreseen in the legislation in relation to labelling exemptions should be followed.

Concerning on-site GMP and GDP inspections, these have been restarted after being postponed or carried out remotely during the pandemic, however, a considerable number of postponed inspections still need to be carried out. The validity of GMP and GDP certificates has currently been extended until the end of 2023, and the GMDP Inspectors Working Group will issue in the coming months an update on the approach for 2024. This Group has also reviewed experiences with remote working arrangements of Qualified Persons during the pandemic and will issue guidance on how those specific arrangements can be applied in the future.

As the CMDh specific practical guidance for facilitating the handling of processes during the COVID-19 crisis and the templates for the submission of applications for COVID-19 exceptional change management process (ECMP) are no longer needed, the CMDh has agreed to remove these documents from the CMDh website.

REGULATION (EC) NO 1234/2008 ON VARIATIONS

The CMDh agreed an update of Chapters 4, 5, 7 and 9 of its Best Practice Guides (BPGs) for the Submission and Processing of Variations in the Mutual Recognition Procedure. A statement has been included in the chapters that the applicant should keep data synchronisation between modules 3-5 and module 1.2 during the procedures and submit an updated application form, each time the dossier information is modified in the context of response submissions. This is in line with the guidance given for new marketing authorisation applications.

- Chapter 4 (tracked)
- Chapter 5 (tracked)
- Chapter 7 (tracked)
- Chapter 9 (tracked)

CMDH POSITIONS FOLLOWING PSUSA PROCEDURES FOR NATIONALLY AUTHORISED PRODUCTS ONLY

The CMDh, having considered the PSURs on the basis of the PRAC recommendations and the PRAC assessment reports, agreed by consensus on the variation of the marketing authorisations of medicinal products containing the following active substances:

- flurbiprofen

MRP/DCP STATISTICS IN THE FIRST SEMESTER OF 2023

Statistics regarding new applications in MRP and DCP in the first semester of 2023 according to the 5-levels of classification of the MRP/DCP Communication Tracking System database will be published on the CMDh website. The statistics will also include information on variation worksharing procedures, referrals to the CMDh and rapporteurships in paediatric worksharing procedures according to Art. 45 and 46 of the Paediatric Regulation.

CMDh January-June 2023 Statistics

Revision of the variation framework - European Commission call for evidence

European Commission has published a Call for Evidence on the revision of the changes to marketing authorisations (Revision of the variation framework for medicines) for consultation. The revision of the Variation Regulation 1234/2008 is included in Annex II to the Commission Work Programme 2023, which also contains the proposed reform of EU pharmaceutical legislation.

The purpose of this initiative is to **make the post-marketing lifecycle management of medicines more efficient, by reducing the administrative burden for the pharmaceutical industry and making better use of regulatory authorities' resources**. This may include a re-classification of some variations into lower categories and/or the introduction of additional flexibility, especially with regard to the level of technical information that must be provided. The initiative will clarify the changes and data to be communicated to the authorities. It also proposes to simplify the single submission or notification of variations (grouping) and work-sharing procedures. Some processes have become increasingly complex from an administrative point of view. This targeted review of the variation system should simplify procedures and eliminate unnecessary administrative complexity. With this revision, recommendations on unforeseen variations under Article 5 of Regulation (EC) No 1234/2008 will be aligned with new requirements from the Regulations on medical devices and in-vitro diagnostic devices (Regulation (EU) 2017/745 and Regulation (EU) 2017/746). The initiative also proposes to extend the risk-based approach to variation categorisation to certain biological medicinal products and to update in particular the rules on biological medicinal products and changes to active substances.
The Regulation will continue to ensure that marketing authorisation holders, competent authorities and the Commission examine the potential impact of the proposed variations on the quality, safety and efficacy of medicinal products in a proportionate way. The initiative will maintain the high level of harmonisation achieved and will strengthen the harmonised approach across the Member States promoting legal certainty and avoiding disproportionate differences in the application of the law.

The main purpose of this call for evidence is to gather insight and contributions from all impacted stakeholders to underpin work on revision of the variation framework for medicines. The feedback given in response to this call for evidence will be fully taken into account, along with the results of previous consultations relating to the Commission proposal for Pharmaceutical Regulation (COM/2023/193 final) and the Commission proposal for the Pharmaceutical Directive (COM/2023/192 final). The Commission will consult the Member States' expert groups and the EMA to gather further evidence and discuss preliminary findings. The Commission will make use of its committees and will organise meetings for consultation purposes.

Multi-stakeholder workshop on RWD quality and experience in use of RWE for regulatory decision-making on 26-27 June 2023 - slides

The slides presented during the multi-stakeholder workshop on RWD quality and experience in use of RWE for regulatory decision-making that took place on 26-27 June 2023 are available here

HERBAL NEWS

EMA HMPC meeting report - July 2023 & HMPC minutes - May 2023

The **report from the EMA Committee on Herbal Medicinal Products (HMPC) meeting held on 17-19 July 2023** has been published.

Among the reported items, the following may be noted:

REVISED EUROPEAN UNION HERBAL MONOGRAPH- DRAFT

The HMPC adopted after systematic review and revision the following draft revised monograph for 3-months public consultation until 15 November 2023:

- Draft revised EU herbal monograph on **Rhodiolae roseae rhizoma et radix**

EUROPEAN UNION HERBAL MONOGRAPHS' REVIEW

Upon recommendation from the Rapporteurs, the HMPC decided after systematic review that no revision is required for the following monographs because **no new data were detected that could change the monograph's content**:

- EU herbal monograph on **Capsici fructus**
- EU herbal monograph on **Melaleucae aetheroleum**
- EU herbal monograph on **Origani majoranae herba**

GUIDANCE DOCUMENTS

The HMPC adopted the

- Concept paper on the development of a **Reflection Paper on modern manufacturing techniques used for herbal preparations** (EMA/HMPC/885124/2022)

Consultation will be open until 15 November 2023.

ASSESSMENTS CLOSE TO FINALISATION

Monograph new – final

- **Cnici benedicti herba**

Monograph revision – draft

- **Pelargonii radix**

Monograph review

- **Ononidis radix**
- **Pilosellae herba cum radice**
- **Polygoni avicularis herba**

In addition, the **EMA HMPC May 2023 meeting minutes** have also been published.

EMA HMPC calls for comments on modern manufacturing techniques

The EMA HMPC has published a concept paper on the development of a reflection paper on modern manufacturing techniques used for herbal preparations for consultation.

Modern technologies for the extraction of plants, which are already used in small scale or research applications or to wider extent in the food or cosmetic industry, are not widely used yet at industrial level for the production of herbal medicinal products (HMPs) and therefore rarely subject in applications for marketing authorisation/registration or herbal-specific guidance. However, the role of modern manufacturing techniques must also be considered for its opportunities and effects on critical quality attributes of HMPs. **The new manufacturing processes include modified extraction methods such as ultrasoundassisted, microwave-assisted, enzymatic-assisted, pulsed electric field, supercritical or subcritical fluid and deep eutectic extraction**. Modern techniques could present various advantages over the conventional approaches, such as higher extraction efficiency, reduction in the use of organic extraction solvents, the usage of nonhazardous solvents, a reduction in the extraction time and the consumption of less energy. They also offer extended tools to obtain extracts of selective composition, i.e. for the targeted extraction or exclusion of specific fractions from the total spectrum of plant compounds for better purity, consistency and standardisation of resulting herbal extracts. In addition to their advantages, these methods may also have some disadvantages linked to various issues of technical reliability, consistency, homogeneity, stability, validation, qualification, documentation, transferability or scale up.

The emergence of modern manufacturing techniques may impact the quality dossier content and assessment needs for HMPs, including aspects of the correspondence/comparability of herbal preparations. Scientific discussions at HMPC on newly available data on supercritical CO2-extracts indicate the need for guidance to be able to address herbal active substances not obtained with conventional solvent extraction in general and regarding comparability between preparations obtained by different manufacturing techniques.

Via this consultation, the EMA HMPC is asking interested parties to provide comments covering the range of modern manufacturing techniques applied to herbal preparations in their current manufacturing practice. **Examples used at the industrial level are of particular interest and will be considered in the development of a reflection paper on this subject. The key issue is to discuss the opportunities and challenges in the application of these modern manufacturing techniques to HMPs and the expectations when they are included in the marketing authorisation/registration dossier**. Furthermore, considerations regarding comparability between various preparations obtained by modern

methods as well as those obtained by traditional manufacturing methods should also be covered. Input by industry and academia will help to discuss the relevance of key parameters associated with certain technologies beyond the conventional ones used for classical solvent extraction, such as solvent and drug extract ratio (DER). Also, testing needs, analytical markers and minimum requirements to ensure and document consistent quality of preparations manufactured with modern technologies will need first a dialogue and basic understanding of principles to support harmonised approaches in caseby-case decisions. Such dialogue appears necessary to embrace innovation and application of modern technologies without any derogations to established quality standards and conventions of Ph. Eur. and EU guidelines in order to ensure high and consistent quality of HMPs.

Comments on this concept paper can be sent by 20 October 2023 taking into account the specific request from the committee for examples and their respective opportunities and challenges and expectations with regards to marketing authorization application.

PHARMACOVIGILANCE

EudraVigilance - New Extension of the pilot of signal detection by MAHs until end of 2024

EMA announced that the **pilot of signal detection in EudraVigilance by marketing authorisation holders was extended until the end of 2024.**

Background: The EU pharmacovigilance legislation requires marketing authorisation holders (MAHs) to continuously monitor data in EudraVigilance (EV) to the extent of their access to the database and to inform forthwith the Agency and National Competent Authorities (NCAs) of validated signals detected in the database. In 2017, in order to streamline this new process the European Commission (EC) agreed to a pilot phase on the implementation of the above-mentioned legal requirements. The pilot started on 22 February 2018 and has focused on a limited number of active substances.

The EMA agreed with the EC to further prolong the pilot in its current form, until the end of 2024. During this period, only those MAHs with an active substance or combination included on the 'pilot list' will have to continue performing signal detection in EudraVigilance for these substances. The EC is undertaking a revision of the Implementing Regulation (EU) 520/2012 and experience from the pilot will be considered.

This new information will be shortly reflected on the EMA signal management webpage. The Agency will continue to support MAHs in their EV signal detection activities. Further information can be found on the EudraVigilance training and support webpage.

FOOD ADDITIVES

EFSA follow-up of the re-evaluation of indigo carmine (E 132) as a food additive

The EFSA Panel on Food Additives and Flavourings (FAF) published its follow-up of the re-evaluation of indigo carmine (E 132) as a food additive.

The Panel concluded that the technical data provided by the interested business operator support an amendment of the specifications for indigo carmine (E 132) laid down in Commission Regulation (EU) No 231/2012, as presented by the recommendations made in the table below.

The Panel concluded that there is no safety concern for the use of indigo carmine (E 132) disodium salts, meeting the proposed revision of the specification, at the reported use levels and submitted analytical data.

The re-evaluation of the safety of indigo carmine (E 132) as a food additive under Regulation (EU) No 257/2010 was completed by EFSA in 2014 (EFSA ANS Panel, 2014). The EFSA ANS Panel confirmed the ADI of 5 mg/kg body weight (bw) per day for indigo carmine (E 132) established by JECFA in 1975(JECFA, 1975) and endorsed by the SCF in the same year (SCF, 1975). In its opinion, the ANS Panel indicated that the ADI was applicable to a material with a purity of 93% pure colouring and manufactured using processes resulting in comparable residuals as material used in the Borzelleca et al. studies (1985, 1986) and Borzelleca and Hogan (1985). In addition, the ANS Panel considered that the EU specifications should be revised in order to restrict the indigo carmine material permitted as a food additive (E 132) to the material for which the ADI is applicable.

Purity	Commission Regulation (EU)No 231/2012	Comment/justification for revision
Name	Indigotine, Indigo carmine	To harmonise the name in the definition to only indigo carmine or indigotine and insert the other as a synonym
Synonyms	CI Food Blue 1	Please see above
Definition	Indigotine consists essentially of a mixture of disodium 3,3'dioxo- 2,20-bi-indolylidene-5,50-disulfonate, and disodium 3,30-dioxo-2,20-bi-indolylidene-5,70-disulfonate and subsidiary colouring matters together with	See consideration of the Panel regarding the calcium and potassium salts and the aluminium lakes

	sodium chloride and/or sodium sulfate as the principal uncoloured components. Indigotine is described as the sodium salt. The calcium and the potassium salt are also permitted. Indigo carmine is obtained by sulfonation of indigo. This is accomplished by heating indigo (or indigo paste) in the presence of sulfuric acid. The dye is isolated and subjected to purification procedures	
Colour Index No	73015	
Einecs	212-728-8	
CAS number		860-22-0 (5,5' isomer)
Chemical name	Disodium 3,3'-dioxo-2,2'-bi-indolylidene-5,5'-disulfonate	Unchanged
Chemical formula	$C_{16}H_8N_2Na_2O_8S_2$	Unchanged
Molecular weight	466,36	Unchanged
Assay	≥ 85% total colouring matters (calculated as sodium salt) ≤ 18% disodium 3,3'-dioxo-2,2'-biindolylidene-5,7'-disulfonate $E^{1\%}_{1cm}$ 480 at ca. 610 nm in aqueous solution	Unchanged
Description Appearance of the aqueous solution	Dark-blue powder or granules Blue	Unchanged
Identification Spectroscopy	Maximum in water at ca. 610 nm	Maximum absorbance* in water at ca. 610nm
Purity		
Water insoluble matter	≤ 0.2%	Unchanged
Subsidiary colouring matters	≤ 1.0% (excluding disodium 3,3' -dioxo2,2'-bi-indolylidene-5,7' -disulfonate)	Unchanged
Organic compounds other than colouring matters –Isatin-5-sulfonic acid –5-sulfoanthranilic acid –Anthranilic acid	≤ 0.5%	Unchanged

Unsulfonated primary aromatic amines	≤ 0.01% (calculated as aniline)	Unchanged**
Ether extractable matter	≤ 0.2% (under neutral conditions)	Unchanged
Arsenic	≤ 3 mg/kg	Maximum limit to be lowered on the basis of the information provided by the IBO and on the considerations of the Panel
Lead	≤ 2 mg/kg	Unchanged
Mercury	≤ 1 mg/kg	Unchanged
Cadmium	≤ 1 mg/kg	Maximum limit to be lowered on the basis of the information provided by the IBO and on the considerations of the Panel

EFSA re-evaluation of calcium carbonate (E 170) as a food additive in foods for infants below 16 weeks of age and follow-up of its re-evaluation as food additive for uses in foods for all population groups

The EFSA Panel on Food Additives and Flavourings (FAF) published its opinion on the re-evaluation of calcium carbonate (E 170) as a food additive in foods for infants below 16 weeks of age and follow-up of its re-evaluation as food additive for uses in foods for all population groups.

In short, the Panel concluded that:

- t**here are no safety concerns with respect to the exposure to calcium carbonate per se at the currently reported uses and use levels in all age groups of the population, including infants below 16 weeks of age.** As a result, **no change to the current conditions of use of calcium carbonate under the EU Food Additives Regulation 1333/2008 are to be expected**.
- the presence of aluminium and other toxic elements should be reduced. As a result, **the EU specifications for E170 under Regulation 231/2012 are expected to be revised as per the table below as part of the Commission regulatory follow up to this opinion.**

The full Panel conclusions are as follows:

- *In this follow-up from the previous re-evaluation of the food additive calcium carbonate (E 170), the Panel concluded that there is no need for a numerical acceptable daily intake (ADI) for calcium carbonate and that, in principle, there are no safety concerns with respect to the exposure to calcium carbonate per se at the currently reported uses and use levels in all age groups of the population, including infants below 16 weeks of age.*
- *With respect to the calcium intake resulting from the use of E 170 in food for the general population and infants <16 weeks of age, the Panel concluded that it contributes only to a small part to the overall calcium dietary exposure.*
- *However, the unavoidable presence of aluminium in E 170 is of concern and should be addressed, in the first instance, by the introduction of a limit in the purity criteria of the EU specifications for E*

170 but also by the reduction of the intake of this toxic element resulting from the dietary exposure to E 170.

- *In addition, the Panel concluded that the technical data provided by the IBO support further amendments of the specifications for E 170 laid down in Commission Regulation(EU) No 231/2012, as presented by the recommendations made in the table below (only lines to be changed are shown).*

	Commission Regulation (EU) No 231/2012	**Comment/justification for revision**
Definition	Calcium carbonate is the product obtained from ground limestone or by the precipitation of calcium ions with carbonate ions	To be included that: E 170 calcium is not an engineered nanomaterial and is not coated or functionalised or with chemically modified surfaces. the source of calcium ions used for the precipitation of calcium carbonate shall be limestone.
CAS number	-	To introduce Limestone: CAS Number 1317-65-3 Precipitated calcium carbonate: CAS number471-34-1
Arsenic	Not more than 3 mg/kg	Maximum limit to be lowered on the basis of the information provided by IBO and on the considerations of the Panel
Lead	Not more than 3 mg/kg	Maximum limit to be lowered on the basis of the information provided by IBO and on the considerations of the Panel
Cadmium	Not more than 1 mg/kg	Maximum limit to be lowered on the basis of the information provided by IBO and on the considerations of the Panel
Mercury	-	Maximum limit to be lowered on the basis of the information provided by IBO and on the considerations of the Panel
Aluminium	-	Maximum limit to be lowered on the basis of the information provided by IBO and on the considerations of the Panel

EFSA timeline update for publication of upcoming scientific opinions

The EFSA timelines for publication of scientific opinions have been updated.

Follow-up opinions on food additives permitted for use in foods for infants and young children:

- Guar gum – E 412 – Dec 2023
- Silicon dioxide – E 551 (Q4 2023/Q1 2024)
- Carrageenan – E407 – 2024
- Citric acid esters of mono and diglycerides of fatty acids – E472c – 2024
- Tocopherols – E306-309 – 2024

Other follow-up opinions:

- Quillaia extract – E 999 – Q4 2023 – jointly with extensions of uses
- Iron oxides – E 172 - 2024
- Gold – E175 – 2024
- Silicates and talc – E552, E 553a,b – 2024
- Vegetable carbon – E153 - 2024
- Silver – E 174 - 2024
- Glutamic acid/Glutamates – E 620-625 - 2024
- Tartaric acid/Tartrates – E 334-337, E 354 - 2024

Re-evaluation opinions:

- Erythritol - E 968 – Oct 2023 - Jointly with application for exemption from labelling
- Neotame – E961 – Dec 2023(?)
- Shellac – E904 – end of 2023 – Jointly with extension of use
- Saccharins – E954 – 2024
- Sucralose – E955 – 2024
- Maltitols – E965 – 2024

Call for technical data on celluloses as food additives (E 460(i), E 460(ii), E 461, E 462, E 463, E 464, E 465, E 468 and E 469)

The European Commission has published on the re-evaluation page a call for technical data on the permitted food additives microcrystalline cellulose (E 460(i)), powdered cellulose (E 460(ii)), methyl cellulose (E 461), ethyl cellulose (E 462), hydroxypropyl cellulose (E 463), hydroxypropyl methyl cellulose (E 464), ethyl methyl cellulose (E 465), cross-linked carboxy methyl cellulose (E 468) and enzymatically hydrolysed carboxy methyl cellulose (E 469).

Information required:

- Analytical data on current levels of lead, mercury, cadmium and arsenic in commercial samples of the food additives. Business operators are requested to submit the analytical results obtained in the context of Article 17(1)5 of Regulation (EC) No 178/20026 during the last 5 years. The results of the individual samples (including sample ID and sampling date) as well as summary statistics (mean, P50, P95, range) are requested. The results should adequately cover the between-batches variability and should be representative of the food additives currently placed

on the EU market. Submission of results from a shorter timespan should be justified. The analyses should be performed with appropriate analytical methods applying state of the art techniques. Specific data on the methods of analysis used should be provided. These include, but are not limited to, the principle of the method, the scope of the method (i.e. the range of sample types that the method is used for), the concentration units used to express the analytical result(s), validation of the method (in particular limit of detection (LOD) and (LOQ).

- The lowest technologically achievable level for lead, mercury, cadmium and arsenic in order to adequately propose maximum limits in the specifications.

The requested data must be submitted no later than **27 October COB**.

STANDING COMMITTEE

General Food Law - 6 July 2023 - Summary report

The **Commission summary report of the Standing Committee on Plants, Animals, Food and Feed – Section General Food Law meeting of 6 July 2023.**

Among others, we may note the following:

- **Exchange of views and possible opinion of the Committee on a draft Commission Regulation (EU) amending Annex II to Directive 2002/46/EC of the European Parliament and of the Council as regards iron hydroxide adipate tartrate used in the manufacture of food supplements.**

A Commission representative presented the draft Commission Regulation which aims to include iron hydroxide adipate tartrate in Annex II to Directive 2002/46/EC and thereby permits its use as a new source of iron in food supplements.

The substance has received a favourable scientific assessment by the European Food Safety Authority and is included in the Union list of novel foods laid down in Commission Implementing Regulation (EU) 2017/2470. During the exchange of views, three Member States noted that a footnote making reference to the novel food authorisation of the substance should be provided for by the draft measure and inserted in Annex II to Directive 2002/46/EC to enable food business operators and control authorities to make the link between the two legal frameworks. The Committee agreed to insert in that Annex a footnote making reference to the Union list of novel foods.

Vote taken: Favourable opinion.

- **Request from Denmark – for an update on the status of the revision of the Food Information to Consumers Regulation, in particular on front-of pack nutrition labelling and the setting of nutrient profiles**

A Commission representative explained that the work to review the Regulation on Food Information to Consumers is ongoing.

Like for all legislative proposals, an impact assessment is being prepared, based on scientific evidence provided by the European Food Safety Authority and the Joint Research Centre, and on consultations with citizens, stakeholders and targeted surveys with Member States, businesses, SMEs, and consumer/health organisations.

Given the complexity of this work, focus is on gathering robust evidence and data, particularly as regards impacts of food labelling on consumer behaviour, given the objective of empowering consumers to make informed, healthy and sustainable food choices.

- **Request from Belgium –working group meetings on maximum amounts of vitamins and minerals in food supplements and fortified foods**

A Commission representative clarified that the last meeting of the task force on maximum amounts took place in March. A working group meeting with all Member States was announced for May to discuss and exchange on the methodology to be followed for setting maximum amounts but the meeting could not take place and no further information can be provided at this stage.

Medical Devices

EUROPEAN UDI WG

Assignment of Unique Device Identifiers for contact lenses - Delegated regulation adopted

The delegated regulation amending the MDR as regards the assignment of Unique Device Identifiers for contact lenses has been adopted.

This delegated regulation has been undergoing public consultation under the feedback procedure available at the following link. In short, this initiative aimed to group highly individualized devices with clear clinical similarities under the identifier called 'Master UDI' in order to have proportionate entries into EUDAMED.

Whilst in the future the Master UDI-DI solution could be extended to other highly individualized devices, at present the focus remains on contact lenses. Should the need arise, the Commission will propose a new delegated act to extend the master UDI-DI solution to other devices.

This regulation shall enter into force on the twentieth day following that of its publication in the OJEU.

It shall apply from 2 years from the date of entry into force of this regulation.

However, manufacturers may already before that date assign a Master UDI-DI in accordance with Regulation (EU) 2017/745 as amended by this Regulation.

MDR IMPLEMENTATION

Notified Bodies Survey on Certifications & Applications - Data dated 31 March 2023

The Commission has published on its website the **"Notified Bodies Survey on certifications and applications (MDR/IVDR)"** based on **data collected from notified bodies until 31 March 2023**.
The complete survey – **accessible here** – is based on data from 39 notified bodies designated under MDR/IVDR.

Pursuant to the data, there are 11418 MDR applications and 2951 MDR certificates (cf. previous survey from Oct. 2022: 8120 applications and 1990 certificates respectively) . The survey gives also an overview on certifications and applications by annex and by type (QMS vs Product). Furthermore, the survey indicates that 311 applications under Rule 14 MDR have been filed and 45 certificates have been issued thereof. The survey also indicates that 2 applications under Rule 21, first indent, have been filed while so far no certificates have been issued thereof (see slide 12).

On average it takes 2-3 month from an application lodged to a written agreement signed taking into account that this is based on the feedback from 33 notified bodies. For 45 % of the submissions, it takes 13-18 months to reach a certificate (QMS+Product) under the MDR (cf. previous survey from Oct. 2022: 82%); for 23 % of the submissions it takes 19-23 months to reach a certificate (QMS+Product) under the MDR (cf. previous survey from Oct. 2022: 18%); for 16 % of the submissions it takes 6-12 months to reach a certificate (QMS+Product) under the MDR (cf. previous survey from Oct. 2022: 0%).

11th NB Designated under IVDR

The **Finland-based notified body 'Eurofins Electric & Electronics Finland Oy Source` has been notified as the 11th Notified Body under the IVDR** (after ~~BSI UK*~~, TÜV SÜD, DEKRA, BSI Group The Netherlands, TÜV Rheinland, DEKRA Certification B.V, GMED SAS, QMD Services GmbH, MDC MEDICAL DEVICE CERTIFICATION, 3EC International).

The **link to the Commission database NANDO** (New Approach Notified and Designated Organisations) is also available for more details.

**Adjustment of designations in the NANDO database: As reminder please note that the designated UK notified body "BSI UK" under the MDR and IVDR, as well as under the current medical device directives, has been removed from the NANDO database given the fact that the EU/UK Brexit withdrawal agreement period came to an end.*

Updated Questions & Answers - Practical arrangements on the companion diagnostics consultation procedure to the EMA by NB

EMA published an **updated Questions & answers document concerning the practical arrangements on the companion diagnostics consultation procedure to the European Medicines Agency by notified bodies** which can be **accessed here**.

Updated EMA document - Questions & Answers on the consultation procedure to the EMA by notified bodies on an ancillary medicinal substance or an ancillary human blood derivative incorporated in a medical device

EMA has published an updated version of their Q&A on the consultation procedure to the EMA by NB on an ancillary medicinal substance or an ancillary human blood derivative incorporated in a medical device.

Regulation 2023/607 - Updated Q&A on Practical Implementation - Flowchart Published

The **Commission has now published the flowchart to the Q&A update on the practical implementation of the extension of the MDR transitional period** that is intended to assist manufacturers and other relevant actors in deciding whether or not a device is covered by the extended transitional period provided for in Article 120 of the MDR, as amended by Regulation 2023/607.

The document can be accessed here.

In particular, the flowchart should help to determine the eligibility, conditions and deadlines for the placing on the market or putting into service of certain devices in accordance with Article 120 MDR.

Overview on Applications for Designation as a NB - Update 24 August 2023

An **update of the overview on the applications for designation as a notified body** (24 August 2023) for the EU Regulations on MDR and IVDR has been published on the EU commission website.

MDR and IVDR Communication Survey Open

Within the activities of the "Communication campaign on MDR and IVDR " carried out by the Commission with the support of an external contractor under the EU4Health actions supporting the implementation of MDR and IVDR (WP 2022), a "**MDR and IVDR Communication Survey" has been launched.**

The objective of this online survey is to better understand the information needs around the EU Regulations on medical devices (MDR) and in vitro diagnostic medical devices (IVDR). Particularly, how the changes in the legislation are affecting the stakeholders that are directly involved and what challenges the stakeholders are facing to ensure a smooth transition to the new regulations.

The survey can be accessed here and is open to the public.

Parliamentary Question - Equal Access to Medical Innovations - Commission Answer

The Member of a European Parliament Sirpa Pietikäinen (EPP, Finland)) submitted **a parliamentary question for a written answer to the European Commission** on 5 July regarding the topic of **ensuring equal access to breakthrough medical innovations for European patients** as reproduced in the following:

> *Equity in healthcare access is a crucial objective for the EU. However, patients with life-threatening or highly debilitating diseases currently face disparities in treatment depending on whether they require medicines or medical technologies. While the European Medicines Agency has established mechanisms for evaluating certain pharmaceutical products on a priority basis, such as conditional marketing authorisations and the PRIME scheme, no equivalent mechanisms exist for medical technologies. This absence of a dedicated priority review process for medical technologies, coupled with the challenges of implementing the Medical Devices Regulation (MDR), contributes to delays in approvals and impedes patients' access to innovative medical devices. Therefore:*
>
> *1. What measures does the Commission plan to take to enhance patients' access to innovative medical technologies and tackle the delays in evaluating new medical devices that were not addressed in the March 2023 MDR amendment regulation?*
>
> *2. Is it considering implementing a priority review process for innovative medical technologies, similar to the existing mechanism for medicines, in order to streamline their evaluation and approval?*

The **answer given by the European Commission** to that question on 12 September is as follows:

> *Regulation EU 2023/607 that has extended the transition periods provided for in Regulation (EU) 2017/745 on medical devices, is accompanied by other measures to ensure the availability of medical devices on the market, as explained below.*

On 25 August 2022, the Medical Device Coordination Group (MDCG) has endorsed a list of mitigating measures that aim to increase the capacity of notified bodies and ensure the availability of medical devices and in vitro diagnostics.

> *Under Action 17 of MDCG 2022-14, the Commission aims to increase the necessary flexibility to apply the reinforced clinical evidence requirements, especially for devices where there is sufficient but incomplete clinical evidence. This action is particularly relevant for innovative devices for which available clinical data is limited.*
>
> *Due to the highly decentralised nature of the medical devices regulatory framework compared to the medicinal products regulatory framework, the priority review process of the market authorisation system of medicinal products cannot be transferred to medical devices. Yet, for medical devices, a pilot project was launched to provide scientific advice from expert panels to manufacturers on the clinical development strategies for high-risk devices, priority being given to innovative devices and devices addressing unmet medical needs. Further, the impact of the regulatory governance structure on innovation in the medical device field is being assessed in the EU4Health funded study on 'regulatory governance and innovation'.*
>
> *The actions outlined above aim to ensure the availability of medical devices. Ensuring patient access to medical devices/medicinal products is also linked to their reimbursement, which is a Member State competence.*

TEAM NB PUBLICATION

Position Paper - Transfer Agreement for Surveillance of Legacy Devices

Team NB has published on its website a **position paper on the transfer agreement for surveillance of legacy devices.**

In particular, **the document specifies the terms of the transfer of the appropriate surveillance activities according to Article 120 (3e) of Regulation (EU) 2017/745 in respect of legacy devices covered by a certificate issued in accordance with Directive 90/385/EEC or Directive 93/42/EEC. This position paper may be accessed online here.**

According to the third subparagraph of Article 120(3e) MDR, an agreement between the manufacturer and the MDR notified body, to which a formal application has been lodged, and, where practicable, the notified body that issued the MDD/AIMDD certificates, must set arrangements for the transfer of the appropriate surveillance in respect to devices covered by the written agreement referred to in Article 120(3c), point (e) MDR.

On this basis, the proposed model agreement specifies the terms and modalities for the transfer of appropriate surveillance from an OUTGOING NB to an INCOMING NB in accordance with the Regulation (EU) 2017/745 and other relevant scheme requirements and ensures the continuity of the activities between the OUTGOING NB and the INCOMING NB in accordance with the said Regulation.

Position Paper - New MDR Transition Timelines and Notified Body Capacity

Team NB has published on its website a **position paper entitled "New MDR Transition Timelines and Notified Body Capacity".**

This position paper may be accessed online here.

The paper discusses why the new transitional periods were necessary and the consequences that notified bodies expect from this change. Furthermore, this paper elaborates on the current status quo of notified body capacity and measures that will help to secure a successful transition.

PLANNED MEETINGS OF MEDICAL DEVICE COORDINATION GROUP (MDCG) AND SUBGROUPS IN 2023

Update (August 2023)

The Commission has updated the **planned meeting dates of the MDCG and subgroups for 2023**.

The updated document is **available here**.

EUDAMED

Production release 2.12 deployed

The EUDAMED Production release 2.12 (Actors registration, UDI/Devices and NBs & Certificates modules) has been successfully deployed.

- EUDAMED restricted
- EUDAMED public

This release brings improvements for all the modules in Production.

See the details in the Release notes and the updated documentation in the EUDAMED Information Centre.

Cross-Sectorial News

EMA ISG - MEETING 26 JUNE 2023

EMA Highlights Published

EMA has published the highlights from the Industry Standing Group (ISG) meeting that took place on **26 June 2023.**

The document may be **accessed here.**

NUTRITION AND HEALTH CLAIMS REGULATION

European Parliament implementation report

The **European Parliament's Subcommittee on Public Health (SANT) is working on an own-initiative implementation report* on Nutrition and Health Claims Regulation (EC) No 1924/2006 (NHCR).** The implementation report is being drafted by The Greens/EFA and it is expected that a draft version will be made available by end-September.

In oder to support SANT in this task, the European Parliamentary Research Service has drafted an internal study titled **Health claims made on foods: Findings on the implementation and application of Regulation (EC) No 1924/2006** which can be accessed here. The study focuses on health claims and use of health claims on foods containing botanicals. Please note that the study itself is prepared for, and addressed to, the Members and staff of the European Parliament as background material to assist them in their parliamentary work. The content of the document is the sole responsibility of its author(s) and any opinions expressed therein should not be taken to represent an official position of the Parliament.

Such European Parliament's own initiative report is usually intended to influence the agenda of the future Commission to be nominated under the next European Parliament's legislature (further to the 6-9 June 2024 European elections).

*In the areas where the treaties give the European Parliament the right of initiative, its committees may draw up a report on a subject within its remit and present a motion for a resolution to Parliament. The own-initative report is not considered a formal decision-making procedure, however, it may inform future policy decisions and legislative initatives as they often contain calls on the Commission to take action.

REQUEST FOR A PRELIMINARY RULING TO THE EUROPEAN COURT OF JUSTICE (CASE C-386-23)

Applicability of NHCR to Botanical Health Claims

The German Federal Court has submitted a **request for a preliminary ruling** to the Court of Justice of the European Union (CJEU) to provide clarity as to whether botanicals in food may be advertised with health claims without those claims being authorized under the Nutrition and Health Claims Regulation No. 1924/2006, pending completion of the evaluation by EFSA and examination by the Commission as permitted health claims notified in respect of botanicals.
This request for a preliminary ruling was **lodged on 26 June 2023** and has been attributed the case number **C-386/23**. Related information and documents of this request are **available here**.

- **Subject Matter in the Main Proceedings**

The plaintiff, the Verband Sozialer Wettbewerb e.V., is a registered association whose responsibilities include the protection of the commercial interests of its members. The defendant distributes the food supplement 'o'gaenics Adapto-Genie ANTI-STRESS-KOMPLEX'. It advertised that product on its website with the health claims about the substances 'saffron extract' and 'melon juice extract, referring among other to "mood-enhancing saffron extract". The plaintiff brought an action before the Landgericht (Regional Court, Germany) and claimed, inter alia, that the defendant should be prohibited from advertising the product 'o'gaenics Adapto-Genie ANTI-STRESS-KOMPLEX' in the course of business with such claims. The Landgericht (Regional Court) upheld the action. The defendant's appeal against that was unsuccessful. The defendant then brought an appeal on a point of-law before the referring court.

- **Question Referred for a Preliminary Ruling**

May plant or herbal substances ('botanicals') be advertised with health claims (Article 10(1) of Regulation [EC] No 1924/2006) or with references to general, non-specific benefits of the nutrient or food for overall good health or health related well-being (Art. 10(3) of Regulation [EC] No 1924/2006) without those claims being authorised under that Regulation and included in the list of authorised claims pursuant to Articles 13 and 14 of the Regulation (Article 10(1) of the Regulation) or without those references being accompanied by a specific health claim contained in one of the lists referred to in Articles 13 or 14 of the Regulation (Article 10(3) of the Regulation), pending completion of the evaluation by the Authority and the examination by the Commission of the inclusion of the claims notified in respect of 'botanicals' in the Community lists referred to in Articles 13 and 14 of Regulation (EC) No 1924/2006?

Background on the proceedings pertaining to a reference for a preliminary ruling: To ensure the effective and uniform application of European Union legislation and to prevent divergent interpretations, the national courts may, and sometimes must, refer to the Court of Justice and ask it to clarify a point concerning the interpretation of EU law, so that they may ascertain, for example, whether their national legislation complies with that law. A reference for a preliminary ruling may also seek the review of the validity of an act of EU law. The Court of Justice's reply is not merely an opinion but takes the form of a judgment or reasoned order. The national court to which it is addressed is, in deciding the dispute before it, bound by the interpretation given. The Court's judgment likewise binds other national courts before which the same problem is raised. It is thus through references for preliminary rulings that any European citizen can seek clarification of the European Union rules which affect him. Although such a reference can be made only by a national court, all the parties to the proceedings before that court, the Member States and the institutions of the European Union may take part in the proceedings before the Court of Justice.
Please note that the average duration of references for a preliminary ruling amount between 15 to 18 months (see statistics concerning the judicial activity of the Court of Justice 2022).

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