Dear Sir or Madam,

Today we would like to inform you about the following topics:

Please pay attention to the following deadlines:

01.01.2019	The German Packaging Act comes into force;
15.01.2019	Reporting deadline for the IFA-notification of verification marks
06.02.2019	Deadline to submit comments on the Draft of the ICH Guideline Q3D M9;
09.02.2019	The EU Falsified Medicines Directive comes into force;
30.06.2020	Deadline to fulfil the requirements of the Analgesics Warning Label Regulation.

We are at your disposal, should you require assistance or have further questions.

Best regards

The DiaMed Team

1 ANALGESICS WARNING LABEL ORDINANCE

The so-called Analgesics Warning Label Ordinance (*Analgetika-Warnhinweis-Verordnung, AnalgetikaWarnHV*)[1], published on the Federal Law Gazette on June 28th, 2018, came into force on **July 1st, 2018**. The aim of the Analgesics Warning Label Ordinance is to limit the risks of the massive use of non-prescription analgesics (**OTC analgesics**) containing the active substances **acetylsalicylic acid**, **diclofenac**, **ibuprofen**, **naproxen**, **paracetamol**, **phenazone or propyphenazone**, to be administered orally or rectally.

The scope of the regulation exclusively applies to OTC products which are authorised for the treatment of **mild to moderate pain or fever**. The regulation does not apply to combination products which contain these ingredients, but are authorized for other/additional indications.

The label should discourage patients to use the these OTC analgesics for a longer time without asking for professional medical advice.

All medicinal products authorised after 1 July 2018 that are affected by the AnalgetikaWarnHV may only be placed on the market if the labelling contains the requested warning:

Medicinal products authorised in accordance to section 21 of the German Drug law and standard marketing authorisations
Bei Schmerzen oder Fieber ohne ärztlichen Rat nicht länger anwenden als in der Packungsbeilage vorgegeben!
(*In the case of pain or fever, do not use for longer than described in the package leaflet without seeking medical advice!)*

Medicinal products in accordance to section 1a no. 8 and 9 of the Ordinance on the Operation of Pharmacies (ApBetrO, magistral and officinal preparations):
Bei Schmerzen oder Fieber ohne ärztlichen Rat nicht länger anwenden als vom Apotheker oder von der Apothekerin empfohlen!
(*In the case of pain or fever, do not use for longer than recommended by the pharmacist without seeking medical advice!)*

The adaptation has to be submitted as a **national change notification** pursuant to § 29 (1) AMG or for German standard marketing authorisation to § 67 (5) AMG. The correct implementation in accordance with section 2 (3) of the AnalgetikaWarnHV should either be confirmed or, alternatively, a labelling draft should be enclosed in the application for variation. It is recommended to submit the change notification via PharmNet.Bund.

Medicinal products authorised before 1 July 2018 that are affected by the AnalgetikaWarnHV may be placed on the market without the required warning for 2 years after the regulation came into force, that is until 30th June 2020.

2 NEW: ICH M9 GUIDELINE ON BIOPHARMACEUTICS CLASSIFICATION SYSTEM (BCS) BASED BIOWAIVERS

The draft of a new EMA multidisciplinary ICH M9 *Guideline on Biopharmaceutics Classification System based Biowaivers*[2] entered the public consultation period in August 2018. The draft of the guideline is now available for download on the EMA website.

[1] Analgetika-Warnhinweis-Verordnung (AnalgetikaWarnHV), 18. June 2018 (BGBl. I S. 864).
[2] ICH Guideline Q3D M9 Biopharmaceutics Classification System (BCS)-based Biowaivers, EMA/CHMP/ICH/493213/2018. Draft Guideline, available at ema.europa.eu.

This guideline is proposed to address the biopharmaceutics classification system (BCS)-based biowaivers. A BCS-based biowaiver shall provide a surrogate for *in vivo* bioequivalence studies. Bioequivalence shall be assumed based on relevant properties of the medicinal product and in particular its active substance, e. g. in the course of generic marketing authorisation applications, extension applications, in early phases of clinical development, variations affecting bioavailability, etc.

BCS-based biowaivers are only applicable for oral immediate release medicinal products with systemically available, highly soluble active substance and adequate therapeutic index (BCS Class I and III drugs).

The guideline discusses parameters and influencing factors that may be used for the justification of a biowaiver. The guideline aims at harmonisation of current regional guidelines/guidance.

The EMA invites to provide comments on the draft to ich@ema.europa.eu until February 6th, 2019, using this template.

3 REGULATORY REQUIREMENTS ASSOCIATED WITH THE FALSIFIED MEDICINES DIRECTIVE

We have extensively described the implications and requirements of the directive in previous newsletters (refer to 30.11.2016, 14.06.2017, 06.10.2017, 27.04.2018).

The countdown has begun for the final phase of the EU Falsified Medicines Directive[3]: On February 9th 2019, the Directive in its conclusive form will go live across Europe, introducing new harmonised measures for the proper control of the medicines supply chain.

The implementation of the regulatory requirements associated with the EU Falsified Medicines Directive, i.e. the text adaptations to comply with sections 17 and 18 of the current QRD template **must be completed by February 9th, 2019** for all authorised medicinal products. Therefore, text adaptations should be submitted as soon as possible.

For existing marketing authorisations, the MAH has the possibility to notify the required text adaptations for inclusion of safety features together with an appropriate regulatory procedure, e. g. a variation (IA, IB or II) or a renewal.

If no regulatory procedures are planned within this timeframe, MAHs are requested to submit a notification pursuant to article 61(3) of Directive 2001/83/EC, provided their products have been approved in a MRP or DCP. These procedures usually take up to 90 days, however, member states are willing to process these procedures in an accelerated manner, if no other changes are submitted. To expedite such assessment it should be confirmed in the cover letter that the only change is to sections 17 and 18 of the QRD template and no other changes have been made. The BfArM indicated that such procedures could be closed on day 6, after a validation phase of usually 5 days.

For nationally approved medicinal products, if there is no further possibility of incorporating the safety feature in a preceding national procedure, the change should be notified according to § 29 (1) AMG. It is recommended to submit the implementation notification via PharmNet.Bund.

[3] Directive 2011/62/EU of June 8th, 2011, amending Directive 2001/83/EC of the Community code, amending to medicinal products for human use. Available at eur-lex.europa.eu.

4 IFA-NOTIFICATION ASSOCIATED WITH THE FALSIFIED MEDICINES DIRECTIVE

As prerequisite for identification of products subject to mandatory verification (i. e. carrying the safety features) in the electronic systems of the supply chain (wholesaler, pharmacies….) and for ensuring that existing merchandise which had been released to the market before 09.02.2019, can be dispensed without obstruction, for each PZN, the so-called verification marks must be reported to IFA

Verification mark (data field)	Meaning	Entry required for products subject to mandatory verification
Verifizierung im Pflichtbetrieb ab Hochladedatum (*Verification during Mandatory Operation from Date of Upload*	Identification of the product as being subject to mandatory verification from effective date, i.e. 09.02.2019 at the latest	(max.) 09.02.2019
Verifizierung im Pflichtbetrieb ab Verfalldatum (*Verification during Mandatory Operation from Date of Expiry)*	Identification of existing merchandise which had been released to the market before the effective date (max. 09.02.2019)	Expiry date of the last batch released to the market prior to the effective date, max. 09.02.2019 + shelf life of the product

Reporting deadline for the timely implementation of reported data in the associated databases is 15.01.2019.

5 REGISTRATION AND REPORTING OBLIGATIONS (GERMAN PACKAGING ACT)

In our newsletter dated 06.10.2017, we already introduced the new German Packaging Act (VerpackG)[4], which will come into force on **January 1st, 2019**.

Registration Requirement (§ 9 VerpackG)
As already indicated in the previous newsletter, from January 1st, 2019, manufacturers are obliged to be registered with the Central Packaging Registry (Zentrale Stelle Verpackungsregister, ZSVR) in the packaging registry called LUCID, before distributing any type of packaged goods.

A registration is possible since the end of August 2018. It can be performed electronically via www.verpackungsregister.org.

Registration requires the following two steps:
1. Application for access to LUCID
2. Entry of registration data

The login should be done within 24 hours via an activation link sent by e-mail; then the procedure must be completed by entering additional information of the manufacturer within 7 days. As part of the registration, the manufacturer must also certify that he has participated in one or more systems or one or more solutions for the packaging sector.

[4] German Packaging Act (*Verpackungsgesetz, VerpackG*), BGBl. I S. 2234. Available online at: www.bgbl.de.

The Central Packaging Registry will send a registration number by e-mail (provisional before January 1st, 2019), and from January 1st, 2019 on, the administrative act of the registration procedure will be automatically issued and electronically transmitted.

Data Reporting Requirement (§ 10 VerpackG)
In addition to registering, manufacturers will also have to immediately transmit packaging-related data to the Central Office. At a minimum, the following data must be reported:

- Registration number (provided by the Central Office before)
- Material and volume of the packaging put on market
- Name of the packaging (recycling) scheme contracted by the manufacturer
- Period of time for which the contract with a packaging (recycling) scheme has been agreed

Unlike with the declaration of completeness (Vollständigkeitserklärung), there will be no *de minimis* threshold for this reporting requirement. Thus, even distributors of small quantities must report their data to the Central Office in accordance with the above specifications.

Since the schemes also have to transmit their corresponding data to the Central Office, simple data comparison will be possible, ensuring a high degree of transparency.

Consequences of non-compliance
If a packaging is not enrolled in the system, it may not be distributed (prohibition of distribution, *Vertriebsverbot*). The registration at the Central Office and the active participation to the system are therefore required by the law. The prohibition of sales concerns both the manufacturer and, by consequence, the retailers. Since the registry is publicly available, both consumers and retailers can quickly check whether the product in question has a sales permission in Germany.

In addition, non-registration or distribution of goods (including offering) by a manufacturer who has not fully registered the packaging, leads to a fine of up to 100.000 EUR per case. The non-participation in a system can be sentenced with a fine of up to 200.000 EUR. In addition, a civil law enforcement of a sales ban by competitors is possible.

Detailed information is available on https://verpackungsgesetz-info.de/en/