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01 REGULATORY, PRICING, AND REIMBURSEMENT OVERVIEW

1. What are the regulatory authorities with jurisdiction over drugs, biologicals, and medical devices in your country?

• **Federal Ministry for Health (Bundesministerium für Gesundheit (BMG), Berlin and Bonn).** https://www.bundesgesundheitsministerium.de/
Drafting legislation, regulations and ordinances in all sectors of health care and social insurance, regarding admission of health care professionals, manufacturing and market licenses for medicinal products and medical devices.

• **Federal Agency for Medicinal Products and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM), Bonn.** www.bfarm.de/EN/BfArM
National manufacturing and market licenses for medicinal products and medical devices, authorization of clinical studies for medicinal products and medical devices, risk supervision, supervision of drug traffic.

• **Robert Koch-Institut (RKI)**
https://www.rki.de/EN/Home/homepage_node.html
The Robert Koch Institute (RKI) is the government's central scientific institution in the field of biomedicine. It is one of the most important administrative bodies for the safeguarding of public health in Germany. Intelligence, prevention, abatement and control of diseases, in particular infectious diseases.

• **Paul-Ehrlich-Institut (PEI)** https://www.pei.de/EN/home/node.html
The Paul-Ehrlich-Institute is another Agency of the German Federal Ministry of Health. Its research and control activities promote the quality, efficacy and safety of biological medicinal products. It is in charge of national market licenses for biomedical medicinal products such as vaccines, authorization of clinical studies and risk supervision regarding medicinal products.

• **Federal Insurance Agency (Bundesversicherungsamt, BVA)**
Supervision of federal public health insurers, administration of structural risk equalization between health insurers, health fonds.

• **Federal Center for Health Education (Bundeszentrale für gesundheitliche Aufklärung (BZgA)**
Prevention campaigns, education measures, model projects for child and youth health, aids, addiction.

• **Institute for Quality and Commercial Feasibility in Health Care (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG)**
Evaluation of diagnosis and therapy methods, cost and benefit evaluations for

medicinal products. review of structured therapy programmes, high quality patient information.

• **Institute for Quality Security and Transparency in Health Care (Institut für Qualitätssicherung und Transparenz im Gesundheitswesen, IQTIG)**)
Development and implementation of measures for quality enforcement and transparent reporting in health care.

Note on English language citations and summaries of German laws, statutes and regulations: As concerns English versions of the laws, statutes and regulations referred to in this publication, please refer to the translations made available on the following website of the Federal Ministry of Justice and Consumer Protection:
http://www.gesetze-im-internet.de/Teilliste_translations.html
References in this publication to English versions and summaries of German laws, statutes and regulations are partly based on the translations made available on above website.

2. What is the regulatory framework for the authorization, pricing, and reimbursement of drugs, biologicals, and medical devices?

1. Medicinal Products, Biologicals:

The regulatory framework for **German manufacturing and market authorizations** of medicinal products and biologicals is set forth in the **German Medicinal Products Act (also referred to as the Pharmaceuticals Act or Drug Act, Arzneimittelgesetz, "AMG") of 12 December 2005 as amended,** as well as a number of supplementary laws and regulations governing the implementation of the rules set forth in the Act. **An English translation of the AMG is available on the following website of the Federal Ministry for Justice and Consumer Affairs:** http://www.gesetze-im-internet.de/englisch_amg/index.html.

European manufacturing and market authorizations by EMA, London, are regulated by EU Regulations, notably Regulation (EC) No 726/2004.
Definition of **Medicinal Products**: Pursuant to § 2 (1) of the Medicinal Products Act, all "substances and preparations made from substances which are intended for use on or in the human or animal body and are intended for use, based on their properties, as remedies for the curing, alleviating or preventing of human or animal diseases or disease symptoms' are medicinal products (Medicinal Products), unless they are foods, cosmetics, tobacco products or medical devices. The rules of the German AMG are essentially based on EU Directive 2001/83 (Code of Human Medicines Directive), EU Regulation 536/2014 and many others.

2. Medical Devices:

The regulatory framework for the manufacture and authorization of medical devices is set forth in the Medical Devices Act (Medizinproduktegesetz, "MPG") of 2 August 1994, as amended, as well as supplementary laws and regulations governing the marketing of medical devices.

3. The regulatory framework of pricing of medicinal products and medical devices

was reformed in 2011 and is essentially governed by the **Law Reforming the Pharmaceutical Market** generally referred to as "**AMNOG**"

(**Arzneimittelmarkt-Neuordnungsgesetz of 2011**), as well as a number of other and supplementary laws and regulations. Up to 2011, the wholesale sale price of a new, patent protected prescription drug was determined by the manufacturer, except where such drug was assigned to a group of fixed price drugs. Since 2011, this applies only to the first year following market authorization. During that first year, any such medicinal product prescribed within the public health insurance system (Gesetzliche Krankenversicherung (GKV)) is evaluated as to its additional benefits as compared to other current standard therapies of the same indication (early benefit evaluation, „Frühe Nutzenbewertung"). If an additional benefit has been determined, the representatives of the GVK and of the manufacturer negotiate a reimbursement amount which is usually lower than the original manufacturer asking price. If there is no such additional benefit, the new drug is subject to a determined fixed price.

Wholesale adds a wholesale margin within a statutory maximum. That wholesale price is the nationwide uniform price charged to drug stores (pharmacies). The pharmacy sales price for prescription drugs (also uniform in Germany) is determined by adding a margin of 3 percent to the wholesale price, plus a fixed pharmacy service compensation of 8.35 Euros, and the value added tax. If the sale is charged to a public heath insurance, the price is reduced by a fixed deduction which is, since 2015, an amount of 1.77 Euros per unit.

The price of freely sellable medicinal products soled in pharmacies or elsewhere is determined by each pertinent seller (for example, herbal teas, plant extracts, vitamines, minerals etc.).

The price of the large number of generica is relatively moderate in Germany, whereas the prices for patent protected medicinal products is relatively high compared to other markets (where lower or no value added tax or different price regulation systems apply). The price difference prompts some German wholsale businesses to import from abroad (parallel imports).

4. The reimbursement of the cost of medicinal products and medical devices is regulated in laws and regulations regarding public health insurance and private health insurance. Details will be outlined in the answers to **questions 10 to 13** below.

3. What are the steps to obtaining authorization to develop, test, and market a product?

1. The third section of the **Medicinal Products Act** (governing manufacturing licenses in §§ 13 to 20d), the fourth section (governing market license in §§ 21 to 37) as well as the sixth section (governing the protection of human subjects and ethincs in clinical testing in §§ 40 to 42b of the Medicinal Products Act) regulate the development, testing and marketing of **medicinal products.** The **Medical Devices Act** provides the corresponding background for medical devices. These statutes describe in detail the application and authorization process, withdrawals, revocations and the resting of the authorization. A "qualified person" must be available to the medicinal product manufacturing facility.

2. Any medicinal product placed on the German market following a marketing authorization from the German authorities or from the European Medicines

Agency (EMA) must have successfully completed **clinical trials** substantiating the efficacy and safety. "**Finished medicinal products**" are manufactured in advance and placed on the market in packaging intended for distribution to the consumer (as defined in § 4 (1) of the German Medicinal Products Act).

Two kinds of medicinal products do not require marketing authorizations (§ 21 (2) of the German Medicinal Products Act), namely (i) medicinal products manufactured in a under a licensed pharmacy (no more than 100 packages per day) and (ii) medicinal products that are intended for use in clinical trials on humans.

Further, pursuant to § 21 (2) No. 6 of the Medicinal Products Act, an exception applies to medicinal products applied to a patient, free of charge, as a matter of compassionate use (to treat a life-threatening disease that cannot be treated satisfactorily with an authorised medicinal product), subject to the rules of the **Ordinance for Compassionate Use (Verordnung über das Inverkehrbringen von Arzneimitteln ohne Genehmigung oder ohne Zulassung in Härtefällen (Arzneimittel-Härtefall-Verordnung – "AMHV") of 14. July 2010** issued by the Federal Ministry of Health (Bundesgesundheitsministerium).

3. As concerns **medical devices**, §§ 4 to 14 of the Medical Devices Act regulate the required properties of medical devices, §§ 15 to 18 govern the role of supervisory authorities and certifications, §§ 19 to 24 concern clinical testing and market authorizations, and §§ 25 to 31 regulate the supervision and risk reporting.

4. What are the approximate fees for each authorization?

1. Depending on the nature of the product, fees and expenses are charged for the decision on the marketing authorization, on the authorization of tissue preparations, on the authorization of medicinal products for advanced therapies, batch releases, the processing of applications, activities in the context of the compilation and evaluation of risks of medicinal products, for the protest procedure against an administrative act issued on the basis of the Act or other services, including independent consulting and information services. The maximum fee for the market authorization as such of medicinal products is EUR 57,500.

2. Regarding the cost charged by the Paul-Ehrlich-Institute for market authorizations of biomedical medicinal products (such as vaccines), detailed information is available on the Institute's website https://www.pei.de/EN/home/node.html.

5. For how long are marketing authorizations/registrations valid? How are marketing authorizations/registrations renewed?

1. Pursuant § 31 of the Medicinal Products Act, a marketing authorisation expires (i) if the authorised medicinal product is not placed on the market within three years from marketing authorisation, or if it was placed on the market but the market presence is interrupted for three successive years; (ii) when waived in writing; (iii) five years after it was granted, unless a timely application for prolongation is filed nine months prior to the expiry date; (iv) if the prolongation of the marketing authorisation is refused. Prolonged marketing authorizations are valid for an unspecified period, subject to detailed conditions.

2. Pusuant § 31 (2) of the Medicinal Products Act, the application for prolongation shall be supplemented by a report giving details of whether, and to what extent, the criteria by which the medicinal product is assessed have altered over the previous five years. Updates of the quality, safety and efficacy documents must be filed.

Further details apply as set forth in § 31 of the Medicinal Products Act.

6. How does the authorization process differ between brand-name products and generic products? Are there differences for local manufacturers versus foreign-owned manufacturers?

1. As concerns German manufacturing and market authorizations, there are no differences in the authorization process for local versus foreign manufacturer, provided all regulatory requirements are fulfilled.

2. Regarding the market authorization of **generic medicinal products**, § 42 b of the German Medicinal Products Act provides for certain limited benefits regarding support document filing requirements. The Act permits the applicant to reference, without a previous applicant's agreement, certain documentation, including the expert report, already filed in support of a previous applicant's medicinal product ("**Reference Medicinal Product**"), provided the Reference Medicinal Product has been authorised for at least eight years. This also applies to filings for authorisations in another Member State of the European Union. However, a generic medicinal product authorised pursuant to this provision facilitating the documentation process may not be placed on the market until ten years have elapsed following the first authorisation of the Reference Medicinal Product (subject to further details). An authorisation pursuant to the above rules requires that the medicinal product in question has the same qualitative and quantitative composition of active substances and the same pharmaceutical form as the Reference Medicinal Product, and that the bioequivalence has been demonstrated in bioavailability studies (details apply). The applicant is not required to submit bioavailability studies if it can otherwise demonstrate that the generic medicinal product meets the relevant bioequivalence criteria in accordance with current scientific knowledge.

7. How are combination products (drug + drug, drug + biologic, drug + device, biologic + device, drug + biologic + device) regulated?

Combination products are usually innovative medicinal products and medical devices featuring the benefits of a medical device in combination with a pharmacological component (based on coating, impregnation or otherwise). The evaluation of a combination product for the regulatory market authorization process of § 25 of the Medicinal Products Act is obviously more complex than the process applicable to a medical device, only. The relevant German authority will require extra time to determine the necessary scope of evaluation and to conduct required examinations. Manufacturers of combination products should, therefore, seek early advice and instructions from the authority to determine the extent of documentation and supplementary approvals or certifications (such as a CE certification).