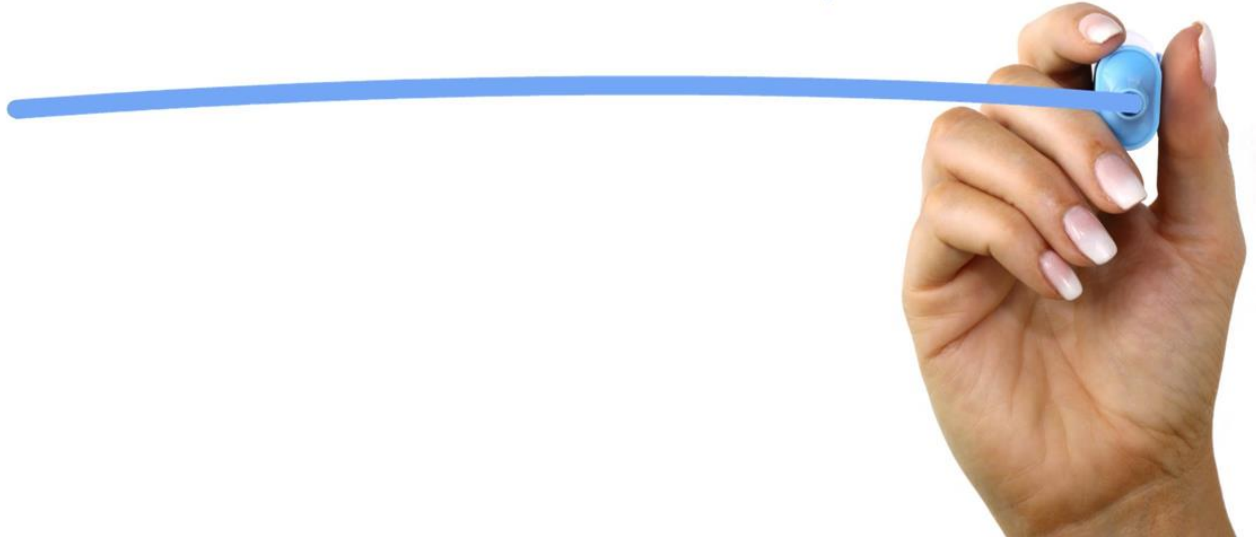


Guideline: Material Compliance (WN9-001)

Guideline to ensure the implementation of Material Compliance requirements during the manufacture of equipment for the pharmaceutical industry

COMPLIANCE



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1 Introduction

The purpose of the B+S Guideline for Material Compliance is to ensure the safe handling of substances and products that are used for the manufacture of pharmaceutical machines or will be installed in them. The guideline describes the requirements of B+S with regard to all known prohibited, regulated and notifiable substances in their current form.

The requirements of the Material Compliance are equivalent to other product requirements.

The guideline includes a summary of the statutory and customer specific requirements taken into consideration at B+S for the product engineering process. It is therefore an internal guideline and must be adhered to by suppliers as well.

Should this standard not yet include amendments, this shall not constitute a release for the supplier from the obligation to comply with the latest version of the statutory requirements, current guidelines and norms/standards. Suppliers are bound to provide these norms/standards, guidelines and rules and regulations on their own responsibility.

The supplier is obligated to comply with the statutory information requirements for product documentation without any cost for B+S. In individual cases, B+S reserves the right to have material tested in a laboratory.

The latest version of this guideline is publicly accessible on our website. The guideline comes into effect with its publication. The suppliers receive a corresponding information in the order documents.

All regulations listed below must be considered independently from each other.

Each individual regulation must be considered in the documentation provided.

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2 Definitions of terms

Battery or Accumulator	Any source of electrical energy generated by direct conversion of chemical energy and consisting of one or more primary battery cells (non-rechargeable) or consisting of one or more secondary battery cells (rechargeable).
CAS Number	The CAS number (also referred to as CAS registration number and CAS registry number - CAS = Chemical Abstracts Service) is an international standard identifier for chemical substances. A unique CAS number exists for each chemical substance registered in the CAS data base (also for bio-sequences, alloys, polymers).
Notifiable Substances	Substances classified as notifiable substances must not be used in some applications and shall be notified if present above the indicated limit values. The mentioned substances must be indicated for each product, component, material, substance preparation, operating supplies. Limits of concentration are specified for the individual substances in the mentioned regulations. A notification is not required if the substance is present in a concentration below these limit values.
Article	Object which during production is given a special shape, surface or design, which determines its function to a greater degree than does its chemical composition.
Homogeneous Substance	A material with a consistently homogeneous composition or a material consisting of a combination of materials, that cannot be disjointed or separated into individual materials by mechanical actions such as unscrewing, cutting, crushing, grinding and abrasive processes (see RoHS - Restriction of Hazardous Substances Directive - art. 3 section 20). Examples of homogeneous substances used at B+S are plastic size parts, parts made of stainless steel 316L conveying the containers, aluminium plates located in the machine base.
Substance	Chemical element and its compounds in the natural state or obtained by any manufacturing process, including any additive necessary to preserve its stability and any impurity deriving from the process used, but excluding any solvent, which may be separated without affecting the stability of the substance and changing its composition (see REACH art. 3 section 1).
Forbidden Substances	Forbidden substances must not be present in products, components, materials, preparations as well as operating supplies at concentrations above the statutory limit values. These substances may only be included in the form of natural impurities. They shall not be added on purpose. The qualitative indication of any impurities with these substances is required.
Packaging	All products made of any materials of any nature to be used for the containment, protection, handling, delivery and presentation of goods, from raw materials to processed goods, from the producer to the user or the consumer. "Non-returnable" items used for the same purposes shall also be considered to constitute packaging (see European Union Directive on Packaging and Packaging Waste, art. 3 section 1).
Packaging Components	Any part of packaging that can be separated by hand or by using simple physical means. Additional elements which are directly attached or fastened to a product and fulfil a packaging function shall be considered to be packaging, unless they are an integral part of the product.

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Preparation A preparation is an intentional mixture (batch, mixture or solution) of two or more substances, e.g. cleaning agent, toner, and colour.

B+S-specific Definitions

Product-carrying parts

All parts of the machine / line, which get in direct (pipe work, hoses) or indirect contact (stopper track) with the product during the filling and closing process.

Non-product carrying parts

All parts of the machine / line, which do not get in contact with the product (parts located in the machine base, for instance).

3 Application

Apart from integration of this guideline into the value-added chain at B+S, it is mainly considered for procurement processes. In filling out the supplier self-disclosure information and within the framework of the regular supplier assessment, each supplier providing products to B+S must confirm in writing that they take into consideration and adhere to this standard. A new confirmation by the supplier is required as soon as one of the below situations has occurred. In such a case, the supplier must within short time provide a new declaration to the purchasing department of B+S:

- products with their ingredients are for the first time delivered to B+S
- correction of wrong declarations
- substances and / or processes of an existing article have been changed
- articles supplied so far have lately become subject to a substance ban and / or substance declaration
- new limit values have been established and one or several articles are concerned
- the mass of the delivered article has changed so that it becomes a notifiable substance
- individual inquiry

The supplier undertakes to follow up on their own responsibility the development of the regulations stated in this document. The declaration requires the written form.

If no base for the limit value is mentioned in this standard or the statutory regulation, an upper limit of 0.1% percentage by weight shall apply.

Depending on the regulation, the limit value refers to the product supplied, the substance, the preparation, the mixture or the homogeneous substance.

Forbidden ingredients shall not be present at concentrations above the limit value in the delivered product. The ban / the limit value may refer to certain applications. Should it not be possible to observe the ban, the concentration must be stated in order to determine the further steps together with B+S. If limit values are mentioned for the substance groups, the supplier must state the relevant individual substances.

4 B+S-specific Regulations

The requirements relating to regulations on substances described in this document are valid for all products installed into pharmaceutical machines under the responsibility of the manufacturer or are designed for installation into these machines. A safety data sheet (SDS) must basically be supplied for each substance / mixture. This document must not be older than 2 years. The SDS must include the substance-specific REACH registration numbers (their own numbers or the numbers of their suppliers), when available.

4.1 GMP Guidelines

The EU directive 2003/94/EC, GMP, Part I, Chapter 3 forms the basis for the definition of product contact parts according to GMP:

The equipment used for the production should not pose a risk for the products.

No equipment part coming into contact with the product may enter into interaction with the product in such a way that product quality is affected, thus provoking a risk, be it a **reactive, additive or absorptive one**.

Strict criteria must be met for the use of material in parts coming into contact with the product. This is the reason why B+S has only approved of the below listed materials for that purpose:

Stainless Steel:	AISI316L (1.4404; 1.4435)
Ceramics:	Aluminium oxide 99.7% Stabilized magnesium zirconium oxide Stabilized zirconium oxide yttrium
Plastic Material:	PEEK (polyetheretherketone) PTFE (polytetrafluoroethylene) PVDF (polyvinylidene fluoride)
Elastomers:	EPDM (ethylene-propylene-diene rubber) FKM (fluororubber) PUR (polyurethane rubber) Silicone

The minimum requirements have been defined and communicated in the

"Bausch + Ströbel Check List of Minimum Requirements with regard to the Declaration of Conformity and the Label on the Packaging for Articles made of Plastics and Elastomers with Product Contact", PR9-018.

Product-contact parts must not contain material components of animal origin, according to the EMA/410/01 guideline.

4.2 REACH Regulation (EC) No. 1907/2006

The use of substances of very high concern in accordance with Appendix XIV according to VO (EC) No. 1907/2006 is related to a procedure for the special approval of a substance. It has to be assumed that the use of the substance will be banned.

Appendix XVII of the REACH regulation includes regulations or bans for precisely defined substances in individual applications.

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The products used at B+S must comply with the requirements of appendix XVII for the Registration, Evaluation, Authorisation and Restriction of Chemicals relating to the applications mentioned therein. The appendix can be accessed via the European Chemicals Agency (ECHA) or the register of the European Community legislation.

All products which contain substances of the candidate list of Substances of Very High Concern (SVHC) at concentrations of > 0.1 % by weight, shall be notified to B+S immediately after identification.

Note: The candidate list is updated every six months.

B+S must be informed about the relevant substances, using the below template.

CAS – No.	Name of substance	Concentration > 0.1% by weight	Which part of the product does contain the substance?

Notifiable substances:

The latest version of the official candidate list of Substances of Very High Concern (SVHC) according to REACH can at any time be accessed with the below link:

http://echa.europa.eu/chem_data/authorisation_process/candidate_list_table_en.asp

According to article 33 of REACH VO, each supplier must provide the following information:

Any supplier of an article containing a substance meeting the criteria in Article 57 and identified in accordance with Article 59 (1) in a concentration above 0.1% weight by weight (w/w) shall provide the recipient of the article with sufficient information, available to the supplier, to allow safe use of the article including, as a minimum, the name of that substance.

Each supplier undertakes to provide all information required according to REACH VO in writing, together with the delivery and without special request. This shall also apply if such substance is only entered into the candidate list during the ongoing supply relationship.

4.3 Chemicals Prohibition Ordinance (“ChemVerbotsV”)

The ordinance on bans and restrictions for the bringing into circulation of dangerous substances, preparations and products according to the Law on Chemical Substances is a federal law in Germany, which stipulates special national requirements in parallel to the REACH regulation. Since REACH as a regulation is directly valid in the EU member states, an amendment of the Chemicals Prohibition Ordinance was adopted in 2016, which unites the requirements of the REACH and CLP regulations with the German Law on Chemical Substances. Furthermore, the national requirements for the following substances and substance groups have been defined in this document:

- Formaldehyde
- Dioxins and furans
- Pentachlorophenol
- Biopersistent fibres

The corresponding requirements resulting thereof may be viewed in the legal text. The Chemicals Prohibition Ordinance entered into force on 1 January 2019 (see: http://www.gesetze-im-internet.de/chemverbotsv_2017/ChemVerbotsV.pdf).

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4.4 2011/65/EU – RoHS

The Directive 2011/65/EU of the European Parliament and of the Council of 8 June 2011 on the restriction of the use of certain hazardous substances in electrical and electronic equipment (RoHS guideline) came into effect on 2 January 2013.

Should products contain substances included in the RoHS guideline, they must be mentioned in the safety data sheet. The area of application is NOT limited to electrical and electronic equipment (EEE). The below substances must therefore ALWAYS be notified when they are contained in products.

No.	Substance with restriction	Limit value in <u>homog. material</u>	Example for exemptions (No. of the RoHS exemption)	No. of the RoHS exemption (only with electri./electro. devices)	% by weight of the substance in homogeneous material
1	Lead and lead compounds	0.1 % by weight	Steel, aluminium, copper (6); refractory filler materials (7); Press-fit connectors (11); enamel print (21)		
2	Cadmium and cadmium compounds	0.01 % by weight	Electrical contacts (8); enamel print (21)		
3	Hexavalent chromium	0.1 % by weight	no exemptions		
4	Mercury and mercury compounds	0.1 % by weight	Discharge lamps		
5	Polybrominated biphenyls (PBBs)	0.1 % by weight	no exemptions		
6	Polybrominated diphenyl ethers (PBDEs/PBDPEs)	0.1 % by weight	no exemptions		

The RoHS regulations on substances refer to the maximum concentrations in the homogeneous material of each article.

4.5 Packaging Directive

The European Parliament and Council directive 94/62/EC of 20 December 1994 on packaging and packaging waste restricts the concentration of heavy metals in packaging. The substances and substance groups of the elements lead, cadmium, mercury and chromium VI must not exceed a maximum weight concentration of 0.01 % by weight (considered cumulatively for all individual elements). In addition to the national and international regulations, the B+S-specific requirements have to be met as well when it comes to the packaging directive. They are either stated in the order documents or are mentioned in the B+S packaging guideline. Apart from protecting the corresponding product, waste prevention and the proper disposal of the packaging must always be taken into consideration. "Oxobiologically" degradable material is to be used as preferred packaging.

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4.6 2006/66/EC – Battery Directive

The Directive 2006/66/EC of the European Parliament and of the Council of 6 September 2006 on batteries and accumulators and waste batteries and accumulators and repealing Directive 91/157/EC restricts the use of mercury and cadmium in batteries and accumulators.

A maximum concentration of 0.0005 % may not be exceeded for mercury and its compounds and of 0.002 % for cadmium and its compounds.

Furthermore, B+S must receive a safety data sheet with instructions for use with regard to safe transport, storage and the conditions of use.

4.7 Conflict Minerals

Raw materials, mineral resources and other natural resources mined in conflict areas or other high risk areas are considered as conflict minerals. Manufacturing or mining of these substances takes place illegally and beyond governmental control. Human rights violations and breaches of international law might be condoned in connection with the exploitation of these materials. It is the aim of B+S to identify articles, which might run the risk of falling into this category, and to make the production chain transparent in cooperation with its suppliers.

From 1 January 2021 onwards, an EU regulation is to make sure that international procurement standards are complied with for the minerals and metals gold, tin, tungsten and tantalum. B+S is anxious to make the supply chain transparent in cooperation with its suppliers and allow for a responsible and conflict-free handling of these materials and minerals.

4.8 Other Substance Restrictions

Type / Group	Example / Comment	Main Source	Indication of the substance and the associated product (part) and the concentration in % by weight
Ozone-depleting substances (ODSs)	CFCs, FCs, etc.	EU: 1005/2009/EC, 842/2006/EC, USA: CAA Tit. VI (42 USC 7671 et seq.)	
Halogens	all types of organic halogens, except for ODSs, e.g. SCCPs (85535-84-8), MCCPs (85535-85-9), etc.	GADSL et al.	
Phtalates	DEHP, BBP, DBP, DINP, DNOP, etc.; state all phtalates even if no statutory regulation exists	1907/2006/EC	
APE / APEO	Alkyl phenol (ethoxylate), e.g. nonylphenoethoxylate (9016-45-9), octylphenol ethoxylate (9036-19-5), etc.	1907/2006/EC	
Asbestos / artificial mineral fibres	Harmful fibres of natural and anthropogenic origin; mainly used for insulation purposes	1907/2006/EC	
Polychlorinated biphenyls (PCBs)	all substances in connection with CAS 1336-36-3	TSCA (15 USC 2605), 40 CFR 761	

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Type / Group	Example / Comment	Main Source	Indication of the substance and the associated product (part) and the concentration in % by weight
Heavy metals in packaging and components	Indicate all heavy metals (Pb, Cd, Cr(VI), Hg), with a content of more than 0.01 % by weight	94/62/EC	
Tetra-, Penta-, Hexa-, Hepta-, Octabromodiphenylether (PBDPE)	The permissible limit value is 0.001 % by weight.	850/2004/EC 757/2010/EC	
PFOS / PFOA	Perfluorooctanesulfonate / perfluorooctanesulfonic acid and its metal salts, halide, amids, etc., including polymers; limit value 0.001 % by weight	2006/122/EC 850/2004/EC 757/2010/EC	
Endocrine disruptors	http://www.epa.gov/endo/pubs/priority_setting/revlist2.htm http://ec.europa.eu/environment/archives/docum/pdf/bkh_annex_01.pdf	EU: BKH Final Rep. Annex 1; US EPA Rev. 2nd List of Chem. for Tier 1 Screening	
PAK (<i>Polycyclic Aromatic Hydrocarbons</i>)	Indicate if the sum of the 18 PAKs >10 mg/kg and if benzo[a]pyrene (50-32-8) or another PAK >1 mg/kg.	1907/2006/EC, US EPA, GADSL	

5 Safety Data Sheets (SDSs)

The SDS is the central element of communication within the supply chain for hazardous substances and mixtures. It provides important information concerning the following characteristics:

- product identity
- occurring dangers
- safe handling
- measures of prevention and in hazardous situations

The requirements with regard to the contents and the format of the SDS are put down in article 31 and the appendix II of the REACH regulation. The supplier of a substance/mixture is responsible that the SDS has been filled in properly and completely.

The SDS must be made available to B+S in the latest version on the day of delivery at the latest (on paper, in electronic form or by giving an information notice with regard to a download option).

Suppliers shall update the SDS immediately (Art. 31(9)) in the below cases:

- new information is available, which might have an effect on risk management measures
- an approval has been given or rejected
- a restriction has been imposed
- The corrected version must be made available to B+S if a delivery took place within the last 12 months.

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Note:

B+S keeps a register of hazardous substances for all substances used and/or stored, which require an SDS. The intended purpose, the point of use and the consumed quantity are entered into this register. The register of hazardous substances is subject to continuous completion and updating.

6 Appendix

- Battery Directive <https://eur-lex.europa.eu/legal-content/DE/ALL/?uri=celex%3A32006L0066>
- Chemicals Prohibition Ordinance https://www.gesetze-im-internet.de/chemverbotsv_2017/
- GMP: <https://eur-lex.europa.eu/legal-content/de/TXT/?uri=CELEX:32003L0094>
- Conflict Minerals http://ec.europa.eu/trade/policy/in-focus/conflict-minerals-regulation/regulation-explained/index_de.htm
- REACH: http://echa.europa.eu/chem_data/authorisation_process/candidate_list_table_en.asp
- RoHS <https://www.ce-richtlinien.eu/rohs-richtlinie-zur-beschaenkung-der-verwendung-bestimmter-gefaehrlicher-stoffe-in-elektro-und-elektronikgeraeten/>
- Packaging Directive <https://www.bmu.de/gesetz/richtlinie-9462eg-ueber-verpackungen-und-verpackungsabfaelle/>