GUIDANCE ON THE USE OF COVESTRO PRODUCTS IN A MEDICAL APPLICATION

1. Purpose

The purpose of this Guidance Document is to provide information regarding the use of Covestro Products in medical applications.

2. Medical Application

As used in this Guidance Document, the term "Medical Application" means the manufacture of a medical device using Covestro Products, which is intended under normal use to be brought into contact with the patient's body (e.g., skin, body fluids, blood, bone dentine, or tissues). Wellness devices intended to be used only for a healthy lifestyle as well as medical devices where a part containing the Covestro Product is used for in vitro diagnostic, or has no contact to a patient's body, or where the contact is only to a patients' intact skin but this is not directly related to the diagnostic, therapeutic or preventative function, are excluded from the definition of Medical Application. Apparatus to manufacture medical devices, medical device primary and secondary packaging and labelling are also excluded from the definition.

The term "Medical Application" also means all stages of manufacture (including apparatus and process chemicals) and primary packaging of pharmaceutical products using Covestro Products. Medical applications where a part containing the Covestro Product has no contact to an Active Pharmaceutical Ingredient, Excipient or any of their intermediates are also excluded from the definition of Medical Application. Pharmaceutical product secondary packaging and labelling are also excluded from the definition.

3. Covestro Products for a Medical Application

The Covestro Products covered by this Guidance Document are fully reacted polymeric materials (e.g., granules and films), reactive raw materials, dispersions, solutions, and non-reactive raw materials sold by any Covestro legal entity (hereinafter "Covestro Products"). There are two types of Covestro Products allowed for use in Medical Applications:

- Those designated as "**General Medical Grade**" are permitted for medical device applications where consecutive contact is to the patient's intact skin (unlimited duration) or to any other body parts and fluids up to 30 days, as well as for primary packaging of pharmaceutical products. Applications involving consecutive contact with or storage of human tissue, blood or other bodily fluids between 30 and 90 days are permitted only if Covestro explicitly agrees in writing.
- Those designated as "**Limited Medical Grade**" are permitted for specific medical applications and durations as described in the Covestro product literature (e.g., Technical Data Sheet). Beyond this, applications are permitted only if Covestro explicitly agrees in writing.

Covestro Products designated as "General Medical Grade" or "Limited Medical Grade" shall not be considered candidates for the following types of Medical Applications unless Covestro explicitly agrees in contractual agreement to sell such products for such applications: (a) cosmetic, reconstructive, or reproductive implant applications; (b) any other bodily implant applications for greater than 30 days; (c)

applications involving consecutive contact with or storage of human tissue, blood or other bodily fluids, for greater than 90 days; or (d) use in an Active Pharmaceutical Ingredient or Excipient.

4. Appropriate Use of Covestro Products

Covestro has not performed clinical medical studies concerning the use of Covestro Products. Moreover, Covestro has neither sought nor received approval from competent authorities in any country for the use of Covestro Products in a Medical Application.

Covestro makes no representations or warranty regarding (and accepts no responsibility for determining) either: (a) the suitability of a Covestro Product for a particular Medical Application or final end-use product or (b) the adequacy of any warning relating to a Covestro Product or Medical Application or final end-use product. The suitability of Covestro Products in each end-use environment is dependent upon various conditions including, without limitation, chemical compatibility, method of manufacture, temperature, part design, sterilization method, residual stresses, and external loads. It is the sole responsibility of the manufacturer of the final end-use product to determine the suitability of any Covestro Products to ensure that the final product:

- performs or functions as intended
- is suitable and safe for its intended use, and
- complies with all applicable regulatory requirements.

It also is the sole responsibility of the manufacturer of the final end-use product to conduct all necessary tests and inspections to evaluate the final product under actual end-use requirements, obtain the applicable regulatory permits and approvals as well as to advise adequately and warn purchasers, users, and/or learned intermediaries (such as physicians) of pertinent risks and fulfill any post market surveillance obligations.

Any decision regarding the appropriateness of a particular Covestro Product in a particular clinical or Medical Application should be based on the judgment of the manufacturer, seller, the competent authority, and the treating physician. Covestro cannot weigh the benefits against the risks and cannot offer a medical or legal judgment on the safety or efficacy of the use of a Covestro Product in a specific Medial Application.

5. Sterilization

The sterilization method and the number of sterilizations cycles a medical device or pharmaceutical product can withstand will vary depending upon type/grade of product, part design, processing parameters, sterilization temperature, and chemical environment. Therefore, the manufacturer of the end-use final product must evaluate each device to determine the sterilization method and the number of permissible sterilization cycles appropriate for actual end-use requirements and must advise adequately and warn purchasers, users, and/or learned intermediaries (such as physicians) of pertinent risks and fulfill any post market surveillance obligations.

During sterilization, using excessive heating, steam autoclaving or boiling water techniques, polyurethane materials may hydrolyze to their corresponding precursor diamines. For example, aromatic polyurethane based on diphenylmethane diisocyanate (MDI) may hydrolyze and produce methylene dianiline (MDA), and aromatic polyurethane based on toluene diisocyanate (TDI) may hydrolyze and produce toluene diamine (TDA). This condition needs to be considered by the device manufacturer in defining sterilization conditions.

6. Test Data and Information

Covestro may agree to provide existing test data and other information about Covestro Products or to perform additional testing of Covestro Products. In so doing, Covestro does not assume any responsibility to determine the suitability of a Covestro Product for a particular Medical Application or final end-use product or to provide adequate warnings; moreover, any agreement by Covestro to provide such data and/or information does not relieve the manufacturer of its sole responsibility to properly evaluate its final end-use product under actual end-use requirements, nor does it relieve the manufacturer of any of its other responsibilities described in this Guidance Document.

7. Re-use of Medical Devices

Covestro does not warrant or represent that those medical devices made from a Covestro Product are suitable for multiple uses. If the medical device is reprocessed and/or labeled for multiple uses, it is the responsibility of the manufacturer and/or reprocessor to determine the appropriate number of permissible uses by evaluating the device under actual sterilization, cleaning, and end-use conditions and to advise adequately and warn purchasers, users, and/or learned intermediaries (such as physicians) of pertinent risks and fulfill any post market surveillance obligations.

8. Special Considerations

Aromatic amines may be generated via water-blown foaming where, by definition, water reacts with aromatic diisocyanates to generate CO2. Normally, these amines react with excess isocyanate groups to form urea, but may also remain as impurities in the final product. Futhermore, over time, polyurethane materials may also partially hydrolyze to their corresponding precursor diamines (see also section 5). These aspects need to be considered in any end-use application.

9. Risk or Failure

There is a risk of failure and adverse consequences with all Medical Applications. There is also a risk of failure and adverse consequences for the use of Covestro products in connection with any Medical Application.

10. Packaging and Labeling

The purchaser of Covestro Products shall be solely responsible for or shall procure that the manufacturer and/or processor of the medical device or pharmaceutical product shall be responsible for (a) the design, production, assembly, packaging and labeling of the medical device or pharmaceutical product which incorporates a Covestro Product and (b) assigning the purpose for which that Covestro Product is to be used. Covestro is not the manufacturer of any of the medical devices or pharmaceutical products and shall, to the extent permitted by law, not be liable as such.

11. Disclaimer of Warranty and Prohibition on Conflicting Oral Representations

1) To the extent permitted by law, COVESTRO MAKES NO REPRESENTATION, PROMISE, EXPRESS WARRANTY, IMPLIED WARRANTY OF MERCHANTABILITY, IMPLIED WARRANTY FOR A PARTICULAR PURPOSE, OR OTHER IMPLIED WARRANTY CONCERNING THE SUITABILITY OF ANY COVESTRO PRODUCT FOR USE IN ANY SPECIFIC MEDICAL DEVICE OR OTHER PRODUCT OR FOR ANY MEDICAL APPLICATION, AND

2) To the extent permitted by law, COVESTRO MAKES NO REPRESENTATION, PROMISE, EXPRESS WARRANTY, IMPLIED WARRANTY OF MERCHANTABILITY, IMPLIED WARRANTY FOR A PARTICULAR PURPOSE, OR OTHER IMPLIED WARRANTY CONCERNING SUITABILITY OF ANY MEDICAL DEVICE OR OTHER PRODUCT MADE, WHOLLY OR IN PART, FROM ANY COVESTRO PRODUCT.

NO COVESTRO REPRESENTATIVE HAS THE AUTHORITY TO MAKE ANY ORAL PREPRESENTATION THAT CONFLICTS WITH ANY PORTION OF THIS GUIDANCE.

12. Responsibility to Forward This Guidance Document

If the purchaser of any Covestro Product is not the manufacturer of the final end-use product, it is the responsibility of the purchaser to forward this Guidance Document to such manufacturer.

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