PD ISO/TR 79:2015

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Reference materials — Examples of reference materials for qualitative properties

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National foreword

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TECHNICAL REPORT

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Reference materials - Examples of reference materials for qualitative properties

Matériaux de référence - Exemples de matériaux de référence pour les propriétés qualitatives

Reference number
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Foreword

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For an explanation on the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the WTO principles in the Technical Barriers to Trade (TBT) see the following URL: Foreword - Supplementary information

The committee responsible for this document is ISO/REMCO, *Committee on reference materials*.

Introduction

In 2007, ISO/REMCO created an ad hoc group (AHG) to investigate the need for guidance on the production of Reference Material (RM) certified for a qualitative property. AHG 01 carried out a gap analysis, contacting 12 organizations and bodies using qualitative RMs and reviewed 13 documents referring to qualitative RMs. Based on this gap analysis, ISO/REMCO decided in 2008 to create a working group (WG) and to entrust it with the drafting of an ISO document.

Due to the limited information submitted in the following years to WG13, the drafting of internationally harmonized guidance turned out to be impossible. Instead, it was decided to focus on an ISO Technical Report (TR), which summarizes the state of the art of the production of qualitative RMs. This TR lists examples of RMs which are either certified for a qualitative property or which can be considered as in-house RMs characterized for a qualitative property. Therefore, many of the RM examples listed here are based on the principles elaborated in ISO Guide 35[1] and ISO Guide 80.[2] The examples represent the experience gathered by various organizations and bodies and their interpretation of qualitative properties, but did not undergo a consensus building process.

In this TR, the following six RM examples are presented:

a) the certification of RMs for their DNA sequences by an ISO Guide 34[3] accredited reference material producer (RMP) (Clause 2);

b) the in-house characterization of organic chemicals as RMs for identification purposes by a laboratory (Clause 3);

c) the identification of a RM biospecimen by an ISO/IEC 17020[4] accredited tissue bank (Clause 4);

d) the development of a reference material for darnel seed identity (Clause 5);

e) the classification and between-sample homogeneity testing of a freshwater cultured pearl (Clause 6);

f) European Pharmacopoeia reference standards for qualitative analysis (Clause 7).

The lack of international standardization in the area of qualitative properties has been recognized by several groups. This includes WG 2 of the Joint Committee for Guides in Metrology (JCGM), officially responsible for the International Vocabulary of Metrology (VIM),[5] which investigates updating and expanding the VIM to cover also qualitative properties. As these discussions are on-going, the terminology used in the various examples presented in this TR may differ, e.g. some groups refer to qualitative properties as nominal properties. Likewise, no agreement has yet been made on international level if the term measurement is limited to quantitative properties or may as well be used for qualitative properties. To foster the readability of this TR, the term *qualitative property* has been given preference and the term *measurement* has been restricted to its use in conjunction with quantitative properties, following the recommendations expressed by the majority of ISO/REMCO delegates during their 37th annual meeting in 2014.

Due to the lack of common guidance on the production of RMs for qualitative properties, the approaches and understanding of terms properly defined for quantitative properties (e.g. homogeneity and traceability) are differently interpreted and applied for qualitative properties by the various organizations and bodies which contributed to this collection of examples. Likewise, the border between qualitative and quantitative properties is differently interpreted. Ordinal properties are perceived by some groups to be restricted to quantitative properties, while others suggest distinguishing between quantitative and qualitative order.

As the predominant aim of this TR is to contribute to the on-going discussion, these differences were on purpose maintained.

During the writing of ISO/TR 79, ISO/REMCO WG 13 identified a number of discussion items, which could not yet be answered with consensus, but which are considered to be crucial in case further efforts will be made to transform this TR into a Guide.

— The expression of confidence related to identification is discussed and in the majority of the cases, no uncertainty is estimated, although experts agree that the probability for a wrong identification forms also part of the result. The identity of an object does not have an uncertainty; however, the assessment of the identity of an object is related to the possibility for misclassification. Ways to estimate the uncertainty of qualitative analysis are especially suggested in the area of DNA sequencing.[6] At the same time, several areas require an assessment uncertainty equaling zero, like e.g. the classification of blood group values.[7]

— Forward/backward DNA sequencing is considered by many experts as an orthogonal method or method free of parameters influencing the result. At the same time, the question is asked what makes DNA sequencing specific.

— Heterogeneity of materials used as RM for qualitative property identification does not necessarily ruin the intended use. Ways are needed to check to which extend for instance inhomogeneity can be accepted.

— A working group at AOAC International developed internationally harmonized guidelines for the validation of qualitative binary chemistry methods.[8] The Guidelines for Validation of Qualitative Binary Chemistry Methods approach the question from the view point of the method. The question whether the RM used in presence/absence testing needs to be certified for a quantitative or qualitative property has not been discussed in this working group so far.

TECHNICAL REPORT **ISO/TR 79:2015(E)**

Reference materials - Examples of reference materials for qualitative properties

1 Scope

This Technical Report summarizes the state of the art of the production and certification or characterization of qualitative property reference materials (RMs).

The need for guidance documents for the production of RMs certified for qualitative properties was recognized by many experts. At the same time, the available information was found to be too immature to develop an internationally accepted guidance document. Additionally, the lack of an international vocabulary for terms and definitions for qualitative properties made it more difficult for the experts from various testing areas to communicate with each other.

ISO/TR 79 summarizes the available expertise. It aims to contribute to the on-going discussion on nominal properties and the production of such RMs. The investigation of nominal properties is referred to differently in various specialized areas (examination, classification, identification, testing, observation, etc.). ISO/TR 79 tries to foster the future development of an internationally harmonized guidance document.

2 Reference materials certified for their DNA sequence

2.1 General

The following is a compilation of the certification approaches applied for three reference materials which were certified for their DNA sequence by the Joint Research Centre of the European Commission, Institute for Reference Materials and Reference Materials (IRMM, Geel, BE).

2.2 Selected examples of certified reference materials

CRM ERM-AD427[9] is composed of plasmid DNA certified to contain certain DNA fragments. It is used for the quantification of Genetically Modified Organisms (GMOs) and the calibration of a defined quantitative Polymerase Chain Reaction (PCR) method. The Certified Reference Material (CRM) contains a plasmid carrying two defined 2'-deoxyribonucleic acid (DNA) fragments. The plasmid calibrant is certified by DNA sequencing for containing two specific DNA targets per plasmid. The number ratio between the two targets is equal to 1, allowing the use as calibrant for relative real-time PCR measurements. The DNA sequence identity has been confirmed by dye terminator cycle sequencing with a negligible error probability for the sequence identification.

CRM IRMM-448[10] is composed of genomic DNA extracted from a microorganism and certified for its DNA identity (with the PCR region of interest verified by DNA sequencing). IRMM-448 is used as positive control in a defined qualitative PCR method for food testing. The CRM consists of a purified and freeze-dried genomic DNA (gDNA) of *Campylobacter jejuni* (NCTC11351). The identity of the gDNA was confirmed by DNA sequence analysis of the ceuE gene, supporting the harmonization and validation of PCR methods by their use as taxonomic controls in PCR reactions. An indicative value for the mass of freeze-dried gDNA is given.

CRM IRMM/IFCC-490[11] is composed of plasmid DNA certified for its DNA sequence (whole sequence). IRMM/IFCC-490 is intended to be used as positive control in quantitative PCR in the area of genetic testing. The CRM consists of purified plasmid DNA (pDNA) pUC18 containing a specific fragment of the human Factor II (prothrombin) gene sequence. It is intended to support the validation and the harmonization of PCR-based methods used for the detection of the mutation in the human prothrombin gene. In all cases, PCR amplification is followed either by restriction enzyme digestion, hybridization

