Austrian
Federal Office for
Safety in Health Care
BASG

Institute Surveillance
Department Clinical Trials
Traisengasse 5, 1200 Vienna, Austria

MEA/INS/CLTR

Clinical investigation with medicinal products and performance evaluation of in-vitro-diagnostics Statistics 2019

The tradition of the annual newsletters on the statistics of clinical studies in the medical device field continues in 2020. Data since 2010 are reflected.

Clinical investigation of medical devices (MDs) and in-vitro-diagnostics (IVDs) have been under the oversight of the Federal Office for Safety in Health Care (Bundesamt für Sicherheit im Gesundheitswesen, BASG) since January 2nd 2006. The reporting obligations, details on the submission and further information can be found on the BASG website and in the specific guidance document (see downloads). Clinical investigations according to §40 para 5 Austrian Medical Devices Act (Medizinproduktegesetz, MPG) do not have a reporting obligation and are therefore also not considered in the statistics presented in the following.

Initial applications

The Austrian Medical Device Act (Medizinproduktegesetz, MPG) differentiates between clinical investigations that require approval ((§40 (2) MPG), those that require notification (§40 (3) MPG) and those that do not require agency involvement (§40 (5) MPG). The nature of the sponsor (e.g. commercial or academic) is not relevant for this differentiation.

Table 1 and figure 1 illustrate the number of clinical investigations and performance evaluations submitted in Austria grouped according to sponsor type (commercial/academic) between 2010 and 2019.

Overall, the number of submissions has declined in comparison to the previous year. Although there has been a slight increase in commercial submission, the number of academic submissions has markedly decreased. Of note, annual submissions, particularly in the academic setting tend to fluctuate considerably.

Sponsor	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
commercial	**46**	**44**	**61**	**55**	**47**	**43**	**38**	**59**	**42**	**47**
Medical device	38	35	54	49	33	39	32	52	38	43
IVD	8	9	7	6	14	4	6	7	4	4
academic	**17**	**38**	**56**	**78**	**50**	**52**	**16**	**35**	**51**	**34**
Medical device	13	31	55	74	44	50	15	33	50	32
IVD	4	7	1	4	6	2	1	2	1	2
Total	**63**	**82**	**117**	**133**	**97**	**95**	**54**	**94**	**93**	**81**

Table 1: Submitted clinical investigations and performance evaluations according to sponsor type (commercial/academic)

Institute Surveillance
Department Clinical Trials
Traisengasse 5, 1200 Vienna, Austria

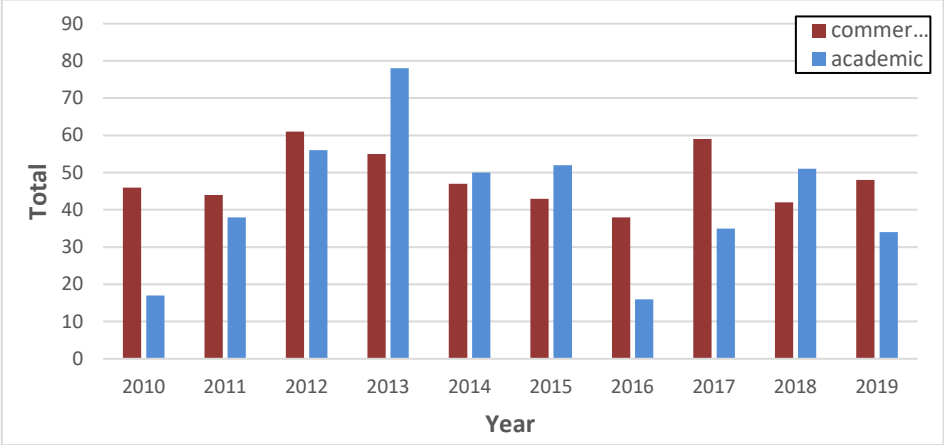

Figure 1: Submitted clinical studies according to sponsor type (commercial/academic)

Table 2 and figure 2 illustrate the submissions grouped according to legal procedure according to MPG and sponsor type.

MPG procedure	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
commercial	**46**	**44**	**61**	**55**	**47**	**43**	**38**	**59**	**38**	**47**
§ 40 (2)	32	28	39	34	25	23	16	25	21	27
§ 40 (3)	14	16	22	21	22	20	22	34	17	20
academic	**17**	**38**	**56**	**78**	**50**	**52**	**16**	**33**	**50**	**34**
§ 40 (2)	5	12	8	13	8	10	3	9	10	12
§ 40 (3)	12	26	48	65	42	42	13	24	40	22
Total	**63**	**82**	**117**	**133**	**97**	**95**	**54**	**92**	**88**	**81**

Table 2: Numbers according to legal procedure

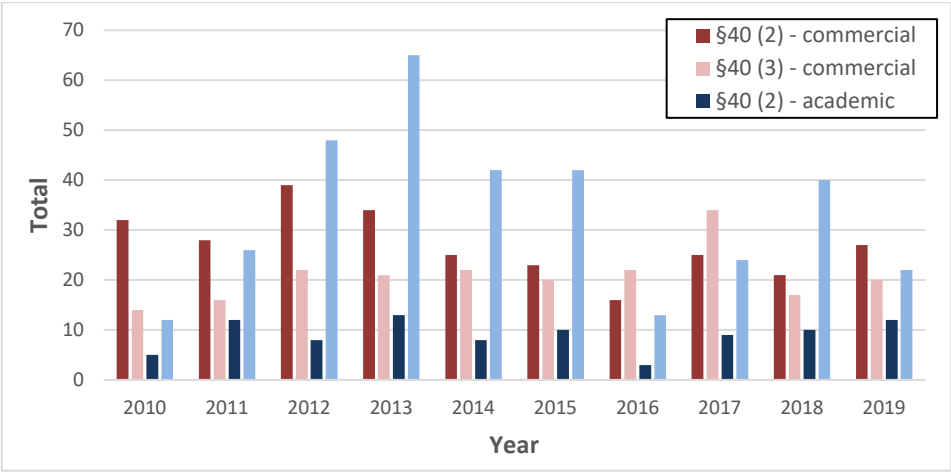

Figure 2: Numbers according to legal procedure

Institute Surveillance
Department Clinical Trials
Traisengasse 5, 1200 Vienna, Austria

Figure 2 illustrates that the number of clinical studies in the high-risk procedure (§40 (2) MPG) have increased, particularly by commercial sponsors. Low risk studies (§40 (3) MPG) have declined particularly in the academic sector.

Table 3 and figure 3 depict the number of clinical studies according to the classification of medical devices as per European legislation. The grouping follows active implantable medical devices (AIMDs) according to Directive 90/385/EEC, medical devices of risk group I to III according to Directive 93/42/EEC and IVDs according to Directive 98/79/EC.

Classification	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**
AIMD	14	7	19	17	15	16	8	11	9	10
class I	1	4	6	12	4	8	4	13	13	5
class IIa	11	13	39	45	28	35	13	25	33	20
class IIb	12	20	23	28	20	16	15	19	18	25
class III	13	22	22	21	10	14	7	17	14	15
IVD	12	16	8	10	20	6	7	9	6	6
Total	**63**	**82**	**117**	**133**	**97**	**95**	**54**	**94**	**93**	**81**

Table 3: Numbers according to classification of the investigated medical device/IVD

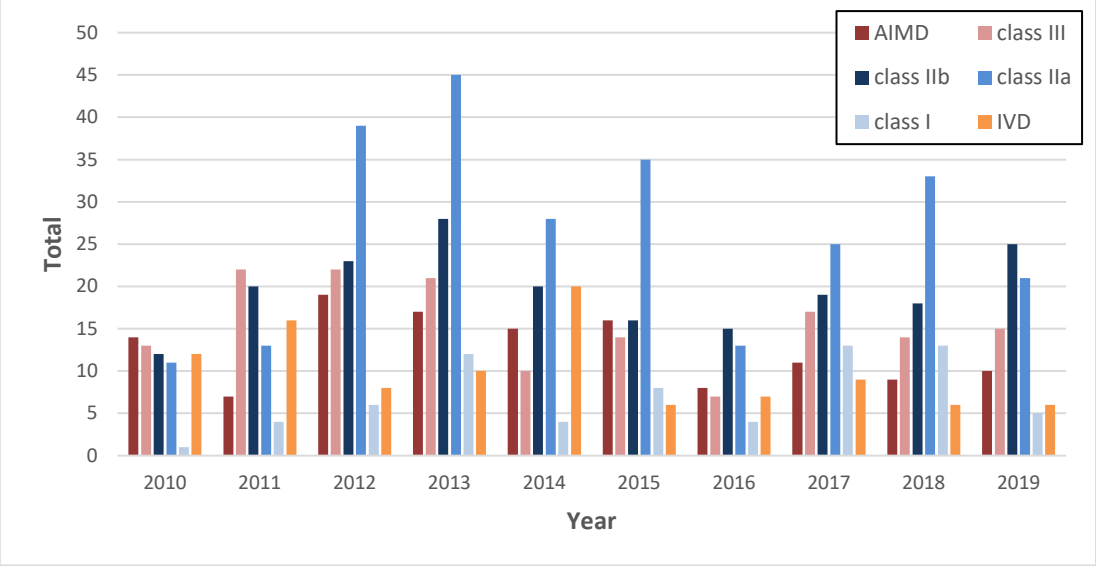

Figure 3: Numbers according to classification of the investigated medical device/IVD

It is apparent, that the majority of clinical studies is conducted with class IIa and IIb investigational products. The ratio between the two has shifted towards class IIb products during the last year.

Considering the number of IVDs and IVD developers on the Austrian market, the overall low number of IVD performance evaluations leads to the conclusion that developers currently rarely conduct independent studies to generate data for clinical evaluation. It is to be expected that the number of performance evaluations will increase significantly with the practical application of the more stringent requirements of Regulation (EC) 746/2017.

Institute Surveillance
Department Clinical Trials
Traisengasse 5, 1200 Vienna, Austria

Medical devices can only be legally introduced to the European market or be put into use, if they fulfill the essential requirements of the European legislation, have undergone the allocated conformity assessment resulting in a declaration of conformity and carry a CE mark.
The scope of clinical investigations/ performance evaluations in case of newly developed medical devices/IVDs (at that stage without CE mark) is to generate initial and pivotal data for clinical evaluation. The conformity assessment builds on these results. The investigation of medical devices/IVDs with CE mark focuses on the investigation of new clinical indications, on comparative studies or requires reporting due to additional study-specific diagnostic or therapeutic measures.

Medical devices/IVDs that do not carry a CE mark can only legally be put into service in the setting of a clinical investigation/performance evaluation (§ 40, except §40 (5) MPG), as a custom-made device (§ 30 MPG), with exceptional authorization (§32 MPG) or, for IVDs, in the setting of an in-house-product (considering essential requirements).

CE-mark	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
commercial	**46**	**44**	**61**	**55**	**47**	**43**	**38**	**59**	**42**	**47**
yes	16	18	26	30	21	24	15	26	20	21
no	30	26	35	25	26	19	23	33	22	26
academic	**17**	**38**	**56**	**78**	**50**	**52**	**16**	**35**	**49**	**34**
yes	9	27	27	44	25	25	8	21	29	25
no	8	11	29	34	25	27	8	14	20	9
Total	**63**	**82**	**117**	**133**	**97**	**95**	**54**	**94**	**91**	**81**

Table 4: Submissions according to certification status of the investigational device and sponsor type

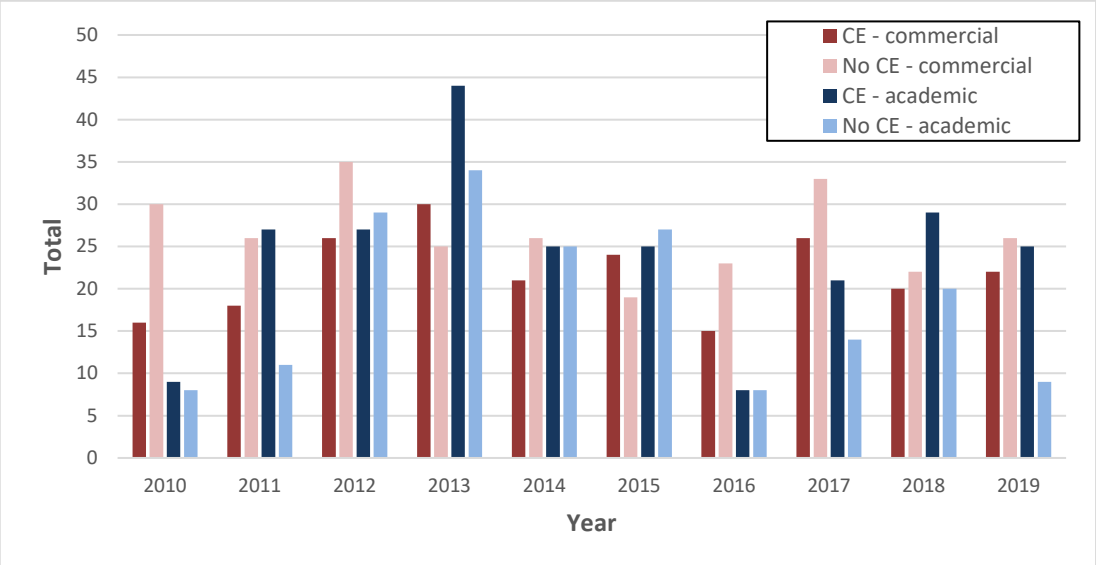

Figure 4: Submissions according to certification status of the investigational device and sponsor type

As illustrated in figure 4, the academic sector mainly conducts studies on CE marked devices to further investigate performance and safety according to the instructions for use or to identify new clinical areas of use. In the commercial sector, the balance between studies on CE marked and non-CE marked devices is

Institute Surveillance
Department Clinical Trials
Traisengasse 5, 1200 Vienna, Austria

more balanced. This could be attributed to the fact that the current legislation permitted in some settings to obtain a CE mark without prior clinical studies and to generate necessary data in a Post-Market Clinical Follow-Up (PMCF).

Substantial and non-substantial amendments

Reporting obligations for sponsors during a clinical study include, amongst others, the reporting of substantial amendments and of Serious Adverse Events (SAEs).

There is a reporting obligation for changes made to the protocol or medical device(s) that have an impact on the safety of study participants or the scientific validity of the study. The annual number of these substantial amendments has remained relatively constant since 2013.

Amendments	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
substantial	39	34	44	69	62	70	62	81	93	75
non-substantial	n.v.*	n.v.*	11	47	49	59	38	30	43	48
Total	**39**	**34**	**55**	**116**	**111**	**129**	**100**	**111**	**136**	**123**

Table 5: Substantial and non-substantial amendments

The reporting of safety data in form of SAEs occurs either as individual reports of cases occurring in Austria or as continuous line listig of all cases up to a given date that occurred within the study in Austria or abroad. According to the MPG, for an SAE, there is no requirement for a causal relationship with the investigated medical device/IVD. This explains the large number of reports and complicates the identification of really relevant events.

The number of SAE reports has been around 3300-3500 annually, whereas there has been an apparent increase. With the practical application of Regulation (EC) 745/2015 a significant drop is to be expected, as the reporting will be restricted to events with a causal relationship and product defects. This is very welcome from the perspective of signal detection.

Year	2010	2011	2012	2013	2014	2015	2016*	2017	2018	2019
SAEs	427	1075	1442	2299	2968	3507	3443	3336	3426	3778

Table 6: Number of SAEs
*since 2016: SAEs from studies with and without reporting obligation to the BASG

Further information

The new Regulations on medical devices (MDR) and IVDs (IVDR) are replacing the framework provided by Directives thus far. They are directly applicable as of May 25th 2017 and do not require an interim translational step into National legislation. Details on the implementation and the transitional period can be found on the website of the Competent Authorities for Medical Devices (CAMD) (www.camd-europe.eu).

The MDR will be applicable as of 26.05.2021 (postponed due to the pandemic) and will be the only applicable legal framework from then on for all newly submitted clinical investigations. Ongoing clinical investigations with medical devices may be continued according to the Directives. Performance evaluations are not yet impacted.

Institute Surveillance
Department Clinical Trials
Traisengasse 5, 1200 Vienna, Austria

The Division for Clinical Trials is actively engaged in the implementation of the new legal framework on a National and European level, for example in the „Clinical Investigation Evaluation Working Group“ of the European Commission. Compared to the medicines sector, a larger number of procedural questions remain to be clarified and guidance documents to be updated or newly written. The National legislation on device studies requires significant adaptation. The Division as a whole is engaged in comments and expert input.

Specific need for clarification is needed on interface issues, such as studies that fall under the scope of both the medicines and medical device legislations, such as drug-device combinations, or the use of IVDs in medicines trial. The European and National discussions require active engagement.
Further information on clinical investigations/performance evaluations can be found in the guidance documents on the BASG webpage (English/German) and are communicated in external talks on an ongoing basis. The presentations of earlier BASG events (“BASG Gespräche”) can be found in the event archive of the AGES academy (see link in downloads)

Downloads and further information:
BASG website MPG/MPG-Guidance document
https://www.basg.gv.at/en/healthcare-professionals/clinical-trials/clinical-trials-with-medical-devices
Competent Authorities for Medical Devices (CAMD)
http://www.camd-europe.eu/
Medical Device Legislative Framework (in EU Languages):
https://ec.europa.eu/growth/sectors/medical-devices/regulatory-framework_en
AGES Academy event archive (mostly in german)
https://www.ages.at/service/ages-akademie/veranstaltungsarchiv/

Contact:
Dr. Stefan Strasser
BASG/AGES
Institute Surveillance
Division Clinical Trials
Tel.: + 43 (0) 50 555-36827
E-Mail: stefan.strasser@ages.at