Clinical Investigation of Medical Devices and Performance Evaluation of In-Vitro-Diagnostics in Austria: Statistics 2018

Division Clinical Trials (CLTR)

The tradition of an annual newsletter on the statistics of clinical investigations/performance evaluations is being continued in 2019. Submissions since 2010 have been considered.

The Federal Office for Safety in Health Care (Bundesamt für Sicherheit im Gesundheitswesen, BASG) has been tasked with the supervision of clinical investigations for medical devices and performance evaluations for in-vitro-diagnostics (IVDs) since january 2nd 2006 through the Austrian Medical Device Act (Medizinproduktegesetz, MPG).
The reporting obligations for all types of studies, details on the submission process and additional information are provided on the BASG Website and outlined in specific guidance documents (see „Downloads“). There are no reporting requirements for clinical investigations according to §40.5 MPG to the BASG and these studies are therefore also not reflected in the statistical presentations.

Initial submissions

The Austrian MPG differentiates between studies that are subject to authorization (§40.2 MPG), studies that have to be notified (§40.3 MPG) and studies without reporting requirement (§40.5 MPG). These requirements are independent of sponsor type and apply to both commercial and non-commercial (academic) studies.

The evolution of clinical investigations and performance evaluations (summarized in the following as clinical studies) in Austria from 2010 to 2018 is presented in table 1 and figure 1 differentiated according to sponsor type (commercial or academic).

In spite of nearly the same number of submissions between 2017 and 2018 there was a detectable shift in the proportion of commercial versus academic submissions. Reduced numbers of commercial submissions were balanced by increased academic submissions.

Obwohl die Anzahl der eingereichten Medizinproduktestudien im Vergleich zum Vorjahr konstant geblieben ist, kam es zu einer Verlagerung der Studieneinreichungen nach Sponsortyp. Es kam zu einem Rückgang der kommerziellen Studien zugunsten eines Anstiegs der akademischen Studien. Nevertheless it has tob e noted that the number of commercial studies was higher in 2017 than in the years prior.

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

Table 1: Clinical investigations and performance evaluations according to sponsor type

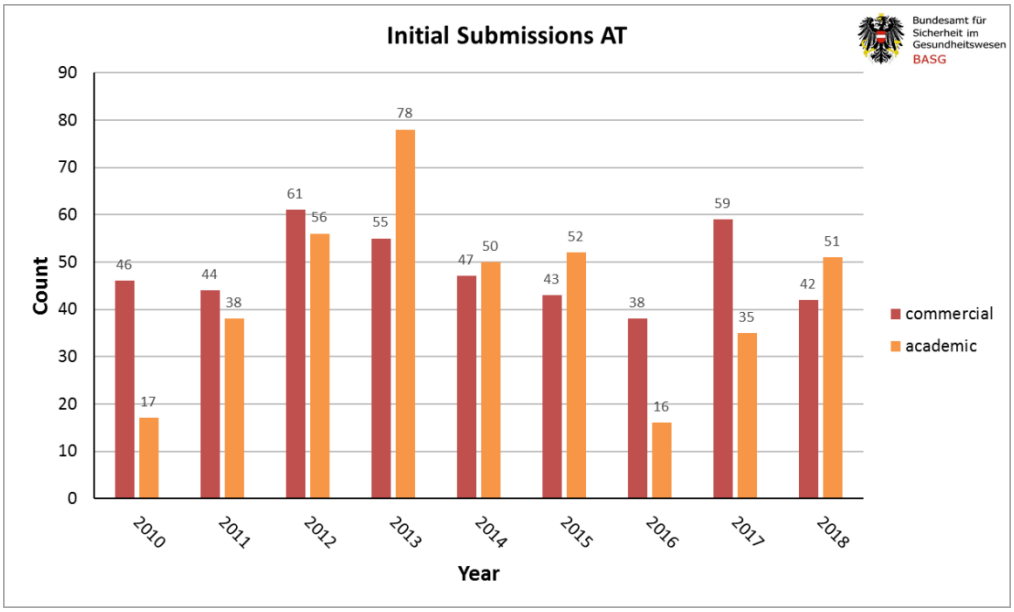

Figure 1: Studies according to sponsor type

The relative increase of academic studies reinstated a comparable proportion of academic studies as in the years 2011-2015 with 54%. In the years 2016 and 2017 the proportion of academic submissions was 30 and 37% respectively, which was mainly due to a decrease of academic studies. The equivalent value for clinical trials with medicinal products so has been relatively stable around 30%, but decreased to 26,1% in 2018.

Year	total	% commercial	% academic
2010	63	73	27
2011	82	53,7	46,3
2012	117	52,1	47,9
2013	133	41,4	58,6
2014	97	48,5	51,5
2015	95	45,3	54,7
2016	54	70,4	29,6
2017	94	62,8	37,2
2018	93	45,2	54,8

Table 2: Proportion of commercial and academic studies

MPG procedure	2010	2011	2012	2013	2014	2015	2016	2017	2018
commercial	**46**	**44**	**61**	**55**	**47**	**43**	**38**	**59**	**42**
§ 40. 2	32	28	39	34	25	23	16	25	21
§ 40. 3	14	16	22	21	22	20	22	34	17
academic	**17**	**38**	**56**	**78**	**50**	**52**	**16**	**33**	**51**
§ 40. 2	5	12	8	13	8	10	3	9	10
§ 40. 3	12	26	48	65	42	42	13	24	40
total	**63**	**82**	**117**	**133**	**97**	**95**	**54**	**92**	**93**

Table 3: Statistics according to procedure

Table 3 and figure 2 illustrate the submitted studies according to the respective procedures of the medical device legislation and sponsor type.

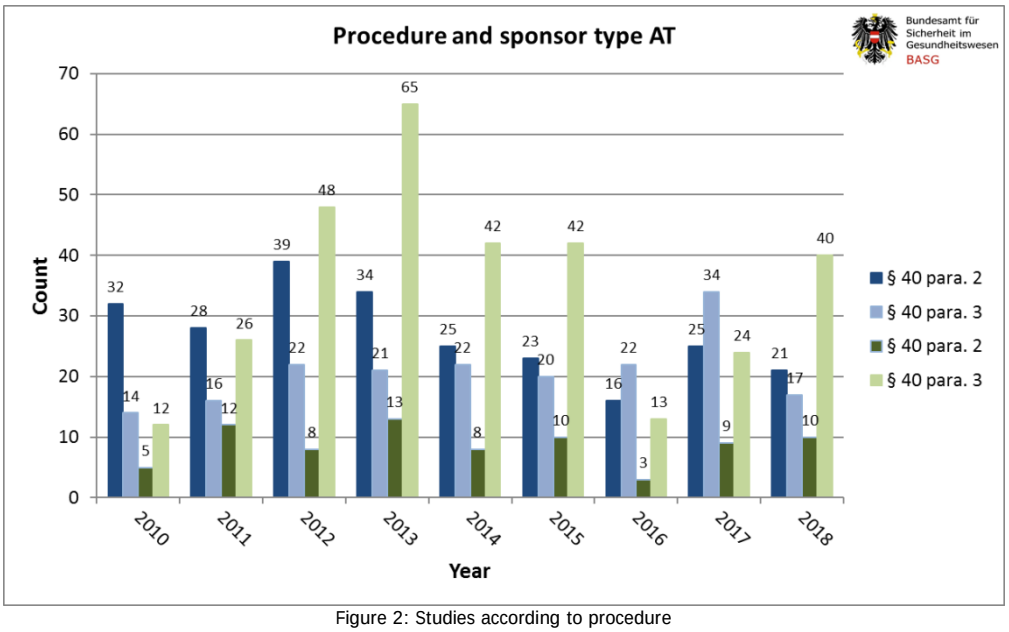

Figure 2: Studies according to procedure
blue columns – commercial studies; green columns – academic studies

Figure 2 illustrates that the decrease in commercial studies last year was mainly due to a decrease in §40.3 MPG studies, while the reduction of §40. 2 MPG studies with 25 to 21 was less pronounced. Studies according to §40.3 constitute the largest proportion in the academic sector and submissions have been increasing again after a low point in 2016.

The distribution of clinical studies according to the risk group of the device investigated according to current EU commission directives is presented in table 4. The devices are classified as active implantable medical devices (AIMD) following Directive 90/385/EEC, devices with risk class I to III according to Directive 93/42/EEC and the In-vitro-device Directive 98/79/EC.

Classification	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
AIMD	14	7	19	17	15	16	8	11	9
Class I	1	4	6	12	4	8	4	13	13
Class IIa	11	13	39	45	28	35	13	25	33
Class IIb	12	20	23	28	20	16	15	19	18
Class III	13	22	22	21	10	14	7	17	14
IVD	12	16	8	10	20	6	7	9	6
total	**63**	**82**	**117**	**133**	**97**	**95**	**54**	**92**	**93**

Table 4: Submissions according to classification of the investigational device

As evident from figure 3 the predominant type of studies are those with class IIa medical devices in all years except 2016, followed by studies with class IIb medical devices. Performance evaluations constituted the lowest share of submissions during the last two years.

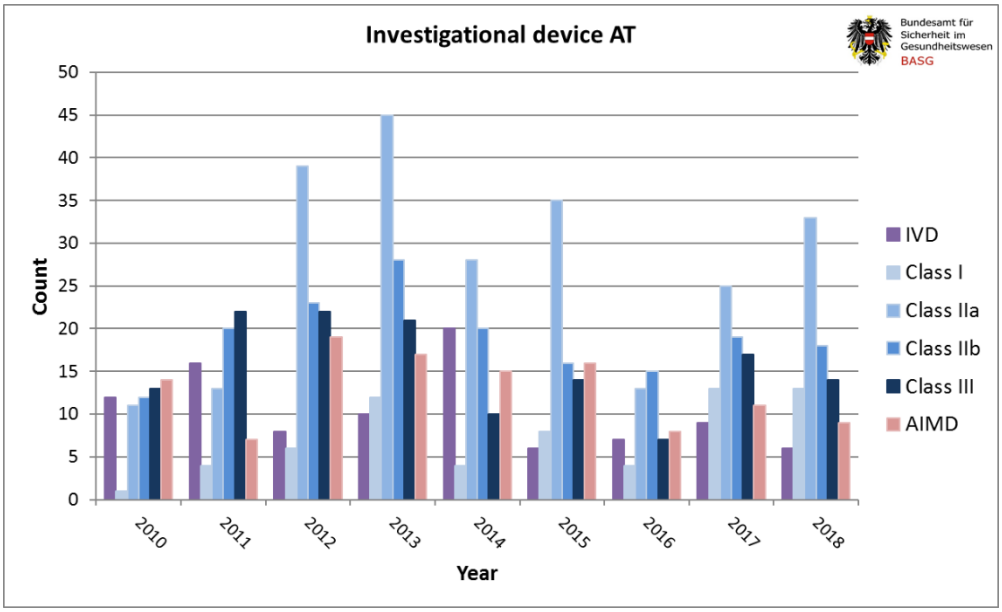

Figure 3: Submissions according to medical device classification

Medical devices need to fulfill the following requirements to be placed on the European market and put into service: The basic requirements of the applicable European directive(s) need to be fulfilled, a conformity assessment has to be conducted leading to a declaration of conformity and they have to bear a CE-mark.

In the case of newly developed medical devices or IVDs clinical studies are predominantly conducted to generate initial or pivotal data for the clinical evaluation as part of the conformity assessment. Clinical studies with devices that bear a CE-mark tend to be performed to evaluate new indications, to conduct comparative studies or to generate data on additional diagnostic or therapeutic measures.

The use of devices without a valid CE-mark is limited to the clinical investigation framework (§40 MPG, except para 5), to custom-made devices (§ 30 MPG), to special exemptions (§ 32 MPG) or to in-house-production, where compliance with the basic requirements is nevertheless required.

CE-mark	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
commercial	**46**	**44**	**61**	**55**	**47**	**43**	**38**	**59**	**42**
yes	16	18	26	30	21	24	15	26	20
no	30	26	35	25	26	19	23	33	22
academic	**17**	**38**	**56**	**78**	**50**	**52**	**16**	**35**	**51**
yes	9	27	27	44	25	25	8	21	29
no	8	11	29	34	25	27	8	14	22
total	**63**	**82**	**117**	**133**	**97**	**95**	**54**	**94**	**93**

Table 5: Studies according to status of the investigational device

Medical devices, where only single components are CE marked, reflected as non-CE marked in the analysis above.

Substantial and non-substantial amendments

The sponsor obligations during the conduct of a clinical investigation include the requirement to report substantial amendments and serious Adverse Events (SAEs).

Changes to the protocol or the medical device that have an impact on the safety of the study participants or the scientific validity of the study need to be reported. The number of substantial amendments has remained relatively constant since 2013.

Amendments	2010	2011	2012	2013	2014	2015	2016	2017	2018
substantial	39	34	44	69	62	70	62	81	100
non-substantial	n.v.*	n.v.*	11	47	49	59	38	30	121
total	**39**	**34**	**55**	**116**	**111**	**129**	**100**	**111**	**221**

Table 6: Amendments

Serious adverse events (SAEs) can either notified as single-reports, for events that occurred in Austria, or as consecutive tabular listing of all events in Austria or abroad. The Austrian medical devices legislation requires reporting of all SAEs independent of the country of origin with the MD or IVD.
Importantly, the classification as SAE according to the medical device legislation is not contingent on a causal relationship with the investigated device. The medical device legislation does not require additional safety-reports.
This is in contrast to the medicinal product framework, where the classification as suspected unexpected serious adverse reaction (SUSARs) includes a suspected causal relationship with the investigated medicinal product. All other events are plotted in the annual development safety update report (DSUR).

The number of SAEs since 2015 has been in the order of 3300 to 3500 reports, including those from studies without reporting obligation (§40.5 MPG).

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

Table 7: Serious adverse events (SAEs)
2010-2015: SAEs from studies with reporting obligation
2016 onwards: SAEs from studies with and without reporting obligation

Further Information

The Medical Device Regulation (MDR) and the In-Vitro-Diagnostics Regulation (IVDR) will replace the existing directives. On May 25th 2017 the regulations entered into force. Details on the implementation and transition periods can be found on the website of the Competent Authorities for Medical Devices (CAMD, link below).

The department for clinical investigations is actively participating in the implementation of new regulatory framework on a National and European level, for example the European Commission's „Clinical Investigation Evaluation Working Group". To a greater extent than in the medicinal product sector, procedural questions still need to be answered and guidance documents as well as other documents need to be written or updated. The National legislation on clinical studies with medical devices requires significant adaptations and the entire division participates in these activities in the form of commenting and expert input.
Particular need for clarification arises at intersectional issues between different legislations, such as studies according to both legislations, products that are drug-device combinations as well as the use of IVDs in clinical trials with medicinal products. European and National discussions require active participation.

Further information regarding clinical studies with medical devices in Austria is presented in the guidance documents (German/English) on the BASG-website (see downloads) and have been transported in external presentations. Presentations held in the context of previous regular stakeholder events, so called "BASG-Gespräche" are accessible via the archive of the AGES-academy (see downloads).

Downloads und weiterführende Information:
BASG Website MPG-Guidance (DE/EN)
Competent Authorities for Medical Devices (CAMD) (EN)
MP-Regularien (EU languages)
Event archive AGES Akademy (DE)