Annex XVI – (EU) 2017/745

Products without an intended medical purpose

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Together with our customers and partners we form the future of medical engineering by pointing out new chances as
well as handling critical challenges.

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NSF is working as an active member in several International standardization working groups like ISO TC 210 and IEC TC 62A.

Therefore, we have influence on standardization politics and decisions.

By co-creating standards, we strengthen companies position against the competition.

This presentation is based on information available as of today and prepared to my Best Knowledge.

This presentation presents my personal understanding of the medical device requirements in the European Union and beyond.

19 Oct 2021

Affected Products (simplified)

- 1. Contact lenses [...] or other (in or on eye).
- 2. Surgically invasive [...]modification of anatomy or fixation of body parts fully or partially inserted into the human body [...].
- 3. Substances, combinations of substances, or articles intended for use as facial or other dermal or mucosal fillers by subcutaneous, submucosal, or intracutaneous injection or other means of introduction, except those for tattooing
- 4. Devices intended for the reduction, removal or decomposition of fatty tissue, such as devices for liposuction, lipolysis or lipoplasty.
- 5. Devices [...] high intensity electromagnetic radiation (infrared radiation, visible light, ultraviolet radiation) [...] such as lasers and devices using intense pulsed light.
- 6. Devices for transcranial stimulation of the brain by electric current or magnetic or electromagnetic fields to alter neuronal activity in the brain.

Scope of regulation (EU) 2017/745, Article 1, 2.

This Regulation shall also apply, as from the date of application of common specifications adopted pursuant to Article 9, to the groups of products without an intended medical purpose that are listed in Annex XVI, taking into account the state of the art, and in particular existing harmonised standards for analogous devices with a medical purpose, based on similar technology.

The common specifications for each of the groups of products listed in Annex XVI shall address, at least, application of risk management as set out in Annex I for the group of products in question and, where necessary, clinical evaluation regarding safety.

Changes possible (EU) 2017/745, Article 1, 5.

Where justified on account of the similarity between a device with an intended medical purpose placed on the market and a product without an intended medical purpose in respect of their characteristics and risks,

the Commission is empowered to adopt delegated acts in accordance with Article 115 to amend the list in Annex XVI, by adding new groups of products,

in order to protect the health and safety of users or other persons or other aspects of public health.

Available Draft Common Specification/Guidance

- Commission Implementing Regulation (EU) ../.. laying down common specifications for the groups of products without an intended medical purpose listed in Annex XVI of in Regulation (EU) 2017/745 of the European Parliament and of the Council on medical devices
  - According to the rolling plan, common specifications for devices without a medical purpose listed in MDR Annex XVI are expected in Q3 2021?
    - → Q4 2021 or even Q1 2022 seems more likely

Common Specification Annex XVI (Draft) – Transition Period Clinical Trial – Article 2

- To be applied 6 months after entry into force (20 days after publication in the OJ of the EU plus 6 months).
- If clinical trials are required, placing on the market/making available/putting into service is granted for plus 3 years if:
  - Products were lawfully placed on the market prior to the effective date of the MD Regulation and continue to comply with the (pre-existing) regulatory requirements AND
  - No significant changes in design and intended use take place AND
  - An application for clinical investigation according to Article 70(1) of the MD Regulation is submitted and accepted within 3 months after entry into force, AND
  - The clinical trial starts within 6 months after the first possible start date (see Article 70(7))
    - (start of clinical investigation after authorization and no negative ethics committee votum)

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(Text with EEA relevance)

Common Specification Annex XVI (Draft) – Transition Period Notified Body – Article 2

- To be applied 6 months after entry into force (20 days after publication in OJ of the EU plus 6 months).
- If involvement of Notified Body necessary (according to Article 52/53 of the MD Regulation), placing on the market/making available/putting into service is granted for plus 1 year.
  - The devices have been lawfully placed on the market prior to the date of application of the MD Regulation and continue to comply with the (pre-existing) regulatory requirements AND
  - No significant changes in design and purpose take place AND
  - By [dd/mm/yyyy+3months = date of application of this regulation + 3 months] a written agreement on conformity assessment is signed by both the notified body and the manufacturer.

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Common Specification Annex XVI (Draft) – Detailed requirements for products

- Annex I - Common Specifications (CS) & General Requirements for all Annex XVI Products
- Annex II - CS Contact Lenses
- Annex III - CS Surgically Invasive - Modification of Anatomy
- Annex IV - CS Facial or other dermal or mucosal fillers by subcutaneous, submucosal, or intracutaneous injection
- Annex V - CS products to reduce, remove, or destroy adipose tissue
- Annex VI - CS for high-intensity electromagnetic radiation
- Annex VII - CS for brain stimulation devices

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Common Specification Annex XVI (Draft) - Scope

- Inclusions according to list Annex XVI
- Exclusions for delimitation e.g.:
- Products that would fit in Annex XVI but are not knowingly marketed in the EU yet, e.g.:
  - Contact lenses with microchips, antennas, etc.
  - Active implantable devices for modifying the anatomy or fixation of a body part.
  - Active devices for subcutaneous filling of the skin or mucous membranes of the face or other areas, submucosal or intradermal injection or other insertion
  - Active implantable devices intended to reduce, remove, or destroy adipose tissue or for which there is insufficient information to establish Common Specifications
- UV treatment (e.g., tanning beds)
- Invasive stimulation (intracranial)

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Annex I – Common Specification General Requirements - Risk Management

Risk management (~ISO 14971:2019, EU-MDR).

- Application of RM process & residual risk according to state of the art (comparable level).
- Responsibility Top management: determine method/risk acceptance & review process for suitability.
- Competent personnel with appropriate qualifications*:
  - Demonstrated experience application of the product concerned OR
  - Demonstrated experience application of equivalent product with no medical purpose OR
  - Demonstrated experience using "analogous device"* with a medical purpose.
  - AND knowledge of the technologies and risk management techniques involved.

* analogous device, equivalence to be demonstrated as per requirement Annex XIV - Clinical Evaluation (technical, biological, clinical equivalence).

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Annex I – Common Specification General Requirements - Risk Management

Risk management (~ISO 14971:2019, EU-MDR)

- Documenting resulting restrictions for categories of users & consumers.
- Method for determining overall residual risk must be reflected in risk acceptance determination (~ISO 14971).
- Known & foreseeable hazards (normal and first failure case (~ISO 14971, other standards if applicable, electrical safety).
- Determination of probability of occurrence (PoH) and extent of damage(SoH) in case of exposure in quantitative or qualitative form (risk) (~ISO 14971)
- Risk control (design, protective measure, Information for safety*, training) (~ISO 14971)

*Information for Safety (consideration of knowledge level of the addressee, working environment)-validation of comprehensibility!

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Annex I – Common Specification General Requirements - Usability & Clinical Data


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Usability:

- Intended purpose & reasonably foreseeable misuse (~ISO 14971).
- Consideration of the characteristics of the user & consumer groups (HCP, trained user or layperson) (~ISO 14971, EN 62366-1).

Clinical data:

- Consideration of clinical data as input to risk analysis and determination PoH and SoH.
- If no (sufficient) data available or generation of relevant data is ethically not justifiable → Risk = SoH and worst case PoH!

Annex I – Common Specification General Requirements – Inputs from PMS (SSCP)

Post-market surveillance:

- Clinical data from collection and review of information about the product from post-manufacturing phases.
- If applicable, from the Safety and Clinical Performance Summary Report*.
- Feedback to Risk Management and adjust/continue to update based on information PMS.
  - New hazards
  - Reconsideration of overall residual risk in case of adjustments
  - Measures

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*A summary report on safety and clinical performance for a device includes, in particular, the position of the device in the context of diagnostic or therapeutic options, taking into account the clinical evaluation of this device in comparison with the diagnostic or therapeutic alternatives, as well as the specific conditions under which this device and its alternatives can be considered (Only for implantable devices and devices of risk class III according to EU MDR).

Annex I – Common Specification General Requirements – Labeling

Labeling

- "for non-medical use only"
- "also for non-medical use"
- No clinical benefit claims
- Expected benefit
- Risk resulting from use/application

Instructions for use

- Categories of users & consumers
- Description of risks/risk evaluation/risk control in clear understandable form to make a decision on whether to be treated with it, have it implanted or otherwise use it.
- Expected performance, expected lifetime and possible necessary follow-up
- References to harmonized standards or common specifications

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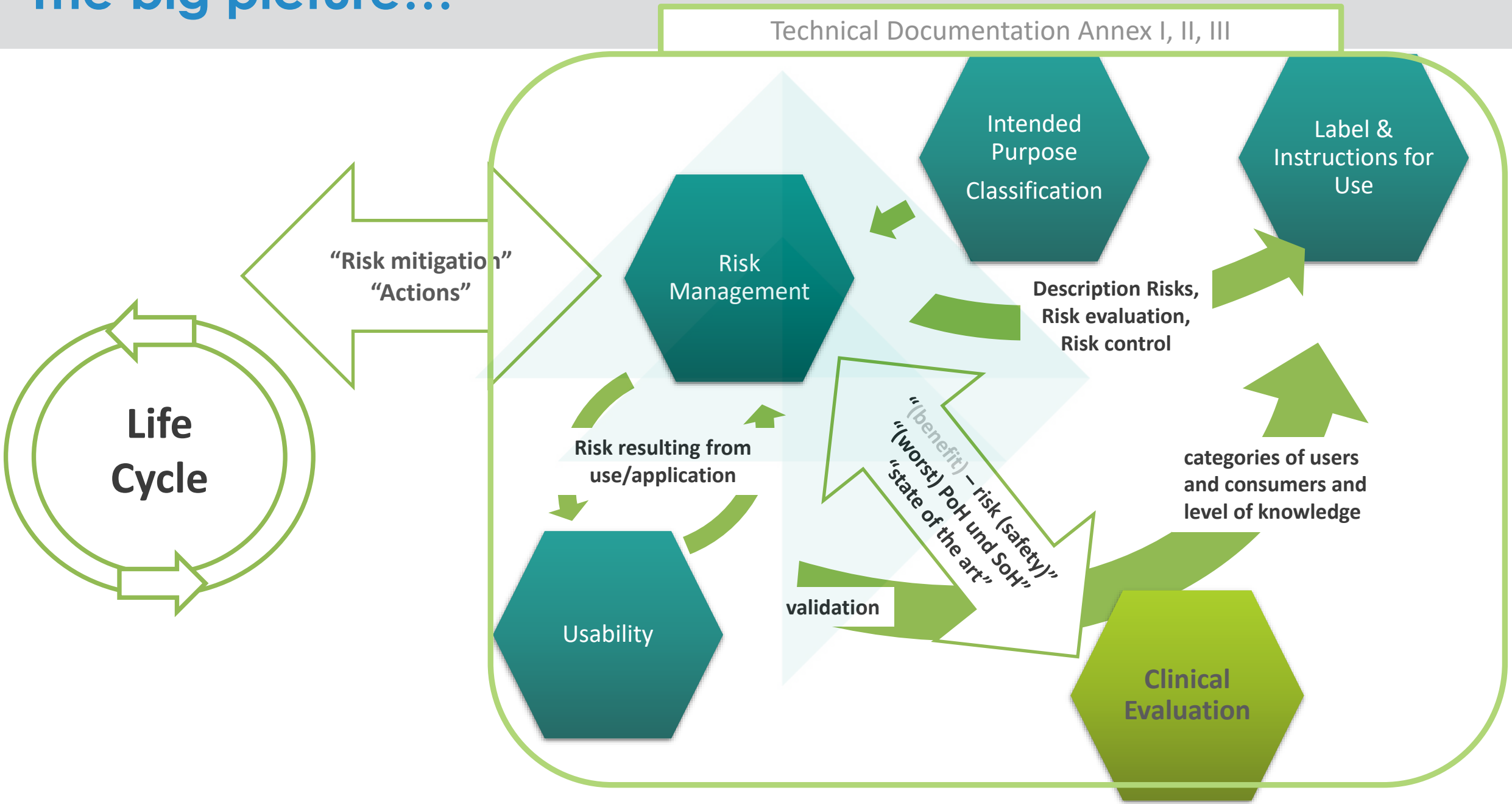
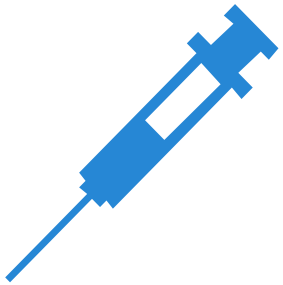
The big picture…



Example Annex IV (Dermal Fillers)

"Substances, combinations of substances, or articles intended for use as facial or other dermal or mucosal fillers by subcutaneous, submucosal, or intracutaneous injection or other modes of introduction, other than those for tattooing"

„Dermal Fillers“



Classification - Annex IV (Example: Dermal Fillers)

- According to Annex VIII, dermal fillers are defined as long-term implantable products.
- They are intended to be fully inserted into the human body through an invasive procedure and to remain in place for more than 30 days after the procedure.
- In addition, these devices contain substances that are wholly or mainly absorbed by the body.
- Given these characteristics, the risk class for most HA- or collagen-based dermal fillers would be class III, the highest classification for medical devices.

ANNEX VIII

CLASSIFICATION RULES

Annex VIII, Rule 8
All implantable devices and long-term surgically invasive devices are classified as class IIb unless they:
— have a biological effect or are wholly or mainly absorbed, in which case they are classified as class III

Example Annex IV – Specific requirements for risk management

Specific risks (exerpt)

Physical and chemical properties of the product	Residues and degradation products, extractable and leachable substances	for non-absorbable products, the risk associated with the removal of the product
the selection of raw materials regarding biological safety, biocompatibility	the specific anatomical location	Injection technique, Type of injection (e.g., rollers, catheters, or needles); force during administration.
the biological safety and biocompatibility of the product	Consumer-specific factors (e.g., previous and ongoing treatments (medical and surgical), age restrictions, pregnancy, breastfeeding)	

Example Annex IV – Specific requirements for risk management

Specific risks mitigation goals & risk control measures (RCM) (exerpt)

unintentional local inflammation/swelling	superficial wounds	capsule formation and contracture
implant visibility through the skin	nerve injury	RCM: Presence of CMR* substances shall be reviewed independently from their concentration!
RCM: Long term effects of non degradable substances originating from the devices.	RCM: Manufacturers shall provide training accessible to the users on the administration and safe use of the device.	

*carcinogenic, mutagenic or toxic to reproduction

Example Annex IV – Specific requirements for Labeling

Specific Requirements - Information for safety (exerpt)

- Ingredients and concentrations, molecular weight, preservatives, etc.
- all residual risks and potential undesirable side effects
- a description of the treatment of the most common side effects, such as overdose, immune responses &recommendation to consult a medical professional
- Influence of the procedure (parallel medication, health condition, etc.)
- number and the volume of the injections as well as the resorption period of the product (specific to each user)
- a clear indication that devices shall not be used in minors
- any contra-indications to the procedure
- “Only to be administered by appropriately trained healthcare professionals who are qualified or accredited in accordance with national law.” (IfU & Label)

Further requirements for manufacturers

- > Determination of the risk classification according to Annex VIII
- > Checking whether the product complies with the MDR and the common specifications for this product group
- > Preparation of technical documentation to demonstrate compliance with regulatory and normative requirements
  - Annex II, III (risk management, suitability for use, clinical evaluation, PMS, labeling)
  - Assessment of whether the existing data situation leads to the necessity of generating clinical data
  - If applicable, in case of drug inclusion (lidocaine etc.) medicinal substance (Directive 2001/83/EC) CTD required.
- > Conformity assessment by Notified Body, Declaration of Conformity and CE Marking
  - Quality management system
  - Integrate regulatory processes

Further requirements for manufacturers

- Assignment of a unique product identifier (UDI) and transmission to the UDI database.
- Submitting key information about the manufacturer, the authorized representative and the importer, if the manufacturer is located outside the EU, to the electronic system (Eudamed).
- Ensure compliance with post-market surveillance and vigilance requirements, e.g., implement field safety corrective actions and report serious incidents to the competent authority.
- Consider requirements for economic operators (importers, distributors, authorized representatives).
- Consider additional requirements for specific devices (Class III implants)
  - Implantation certificate (Article 18 EU-MDR)
  - Summary Safety and Clinical Performance Report (SSCP) (Article 32-EU MDR)
  - Instructions for use - SSCP reference

Annex IV requirements - Summary

- General and product-specific requirements (CS are generally more specific than standards).
- Existing standards on risk management, usability and perhaps product specific standards for analogous devices could cover most of the requirements if applied.
- Life cycle system to be implemented
  - Intended use
  - Labeling
  - Risk management
  - Clinical data
  - Observation of market phase
  - Ongoing observation
- Requirements analogous to medical devices (some add additional burden compared to medical devices?)

Annex IV – To Do for Manufacturers

- Assess your portfolio and the classification for each product.
- Review / assess existing data and evaluate whether it is sufficient or clinical data needs to be generated. Literature data often general but delivers no specific information.
- Implement or update a QMS according to EU-MDR (~ISO 13485) if not available.
- Implement the necessary regulatory processes (Clinical, PMS, Risk, Regulatory Oversight)
- Create a quality plan for implementation and start implementing the requirements in a timely manner.
- Contact and contract a Notified Body.
- Even if the Common Specification is not yet final, you should start now!

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Thanks for your attention!